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PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

187574 Ben-Zvi, Zvi; Burstein, Sumner. Worcester Foundation for Experimental Biology, Shrewsbury, MA 01545 **7-Oxo-delta1-tetrahydrocannabinol: a novel metabolite of delta1-tetrahydrocannabinol.** Research Communications in Chemical Pathology and Pharmacology. 8(2):223-229, 1974.

Incubation products of delta1-tetrahydrocannabinol (THC) with rat liver microsomes were carefully analyzed, and the presence of a hitherto unidentified metabolite was revealed. Mass spectral data suggest a 7-oxo derivative and lithium aluminum hydride reduction of this product gave 7-hydroxy-delta1-tetrahydrocannabinol, substantiating this assignment. Such an aldehyde is a likely intermediate in the detoxification of delta1-THC, which leads to acidic products. 9 references. (Author abstract modified)

187577 Forist, Arlington A.; Pulliam, Albert L.; Kaiser, David G. Research Laboratories, Upjohn Company, Kalamazoo, MI 49001 **N-(2-(diethylamino)ethyl)-2-(p-hydroxyphenoxy)-acetamide, a metabolite of mefexamide in man.** Research Communications in Chemical Pathology and Pharmacology. 8(2):385-388, 1974.

A metabolite of mefexamide, N-(2-(diethylamino)ethyl)-2-(p-methoxyphenoxy)-acetamide, excreted in human urine was characterized as N-(2-(diethylamino)ethyl)-2-(p-hydroxyphenoxy)- acetamide on the basis of its pH partition behavior, TLC mobility, reaction with diazotized sulfanilic acid and its IR and mass spectra. This metabolite is excreted both free and as a glucuronide conjugate. 3 references. (Author abstract)

187805 Seeman, P.; Machleidt, H.; Kahling, J.; Sengupta, S. Department of Pharmacology, University of Toronto, Toronto, Ontario M5S 1A8 **A new prolonged-acting type of chlorpromazine: behavioral effects and prolonged actions on nerve membranes.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):558-565, 1974.

A new type of phenothiazine (a chlorethyl derivative of chlorpromazine), not previously synthesized, and its sustained effects on nerve and erythrocyte membranes were studied. The drug, 2-chlor-10-(3-(beta-chlorethyl)-methylaminopropyl)-phenothiazine hydrochloric acid, stabilized human erythrocytes (from hypotonic hemolysis) in the micromolar concentration range and had prolonged nerve blocking potency. A 14C labelled form of the drug was found to adhere persistently to both erythrocyte and brain synaptosome membranes. In animal behavior tests, the drug was about one fourth the potency of chlorpromazine. There is a possibility that the drug may have some long-term action since the animals recovered more slowly from the antiamphetamine action of the drug than from the antiamphetamine actions of chlorpromazine. 48 references. (Author abstract modified)

187937 Witiak, Donald T.; Hsu, Song Y.; Ollmann, James E.; Griffith, Robert K.; Seth, Shiv K.; Gerald, Michael C. Division of Medicinal Chemistry, College of Pharmacy, Ohio State University, Columbus, OH 43210 **D-(R)- and L-(S)-3-alkylaminopyrrolidino-substituted dihydrodibenzo(b,f)- and -(b,e)thiepins, xanthenes, and diphenylmethanes.** Journal of Medicinal Chemistry. 17(7):690-696, 1974.

Chiral aminopyrrolidines are discussed. It is felt that based upon classical structure - activity relationships, chiral aminipyrrolidines may exhibit a variety of central and peripheral actions. Analogs of known absolute configuration were synthesized to assess stereoselective differences in antipsychotic (neuroleptic), antidepressant, antiParkinson, antihistaminic, and anticholinergic activities. Fewer stereoselective differences were observed. Within this series, dihydrodibenzo(b,f)thiepins appear to serve as the better lead for the future design of antipsychotic drugs. Structural requirements for H1 histamine antagonists in vitro are discussed. 39 references. (Journal abstract)

187938 Rogers, M. E.; Sam, Joseph; Plotnikoff, N. P. Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi, University, MS 38677 **3-Aryl-3-hydroxyquinolizidines with potential hypotensive, antidepressant, and analgetic activity.** Journal of Medicinal Chemistry. 17(7):726-729, 1974.

The synthesis, structure elucidation, and pharmacological evaluation of some 3-aryl-3-hyroxyquinolizidines as semirigid phenethylamines are described. Some antidepressant and analgesic activity was noted in several of the derivatives; no marked blood pressure effects were observed. 11 references. (Journal abstract)

187939 Vida, Julius A.; Samour, Carlos M.; O'Dea, Mary H.; Wang, Theodore S. T.; Wilbur, William R.; Reinhard, John F. Kendall Company, Lexington, MA 02173 **Analgesics. I. Selected 5-substituted 5-propionoxybarbituric acids.** Journal of Medicinal Chemistry. 17(7):732-736, 1974.

Several 5-substituted 5-propionoxybarbituric acids were synthesized and evaluated for analgesic activity. One compound, 5-propionoxy-5-(1-phenylethyl)barbituric acid (29), displayed better analgesic activity than codeine orally and had half the analgesic potency of morphine when administered subcutaneously. Compound 29 constitutes the first example of a potent analgesic lacking a basic center (of pKa permitting extensive protonation at physiological pH). 16 references. (Journal abstract)

187940 Archibald, John L.; Freed, Meier E. Research Division, Wyeth Laboratories, Inc., Radnor, PA 19087 **1,4-Bis(2-indol-3-ylethyl)piperazines.** Journal of Medicinal Chemistry. 17(7):745-747, 1974.

A previously described series of 1,4-bis(2-indol-3-ylethyl)piperidines possessing antihypertensive and central nervous system depressant activities is extended to include 1,4-bis(2-indol-3-ylethyl)piperazines. In general, the pharmacological outcome of replacing a piperidine by a piperazine ring in the compounds was to enhance central nervous system effects. Considerable control of the ratio of CNS and CVS activities was accomplished through variation of the number and positions of alkyl substituents in the indole and piperazine rings. 10 references.

187941 Zweig, Jonathan S.; Castagnoli, Neal, Jr. Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94143 **Chemical conversion of the psychotomimetic amine 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane to 5-hydroxy-2,6-dimethylindole.** Journal of Medicinal Chemistry. 17(7):747-749, 1974.

Interest in the metabolism and mechanism of action of the psychotomimetic compound 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane(4), commonly called DOM, and the structural analogy between 6-hydroxydopamine and the bis-O-demethylated compound 5, a potential metabolite of amine 4, has led to preparation of the p-hydroquinone 5 as an aid to its identification in the urine of animals treated with 4 and in tissue homogenates of 4. Data suggest that the intermediate solution may be an equilibrium mixture of quinone 6 and quinoneimine 8. 16 references.

187942 Kovac, T.; Kajfez, F.; Sunjic, V.; Oklobdzija, M. Compagnia di Ricerca Chimica S. A., Chiasso, Switzerland **3-Onium derivatives of 1,4-benzodiazepin-2-ones with tertiary organic bases.** Journal of Medicinal Chemistry. 17(7):766-769, 1974.

A preparation is described of a new set of hydrophilic 3-substituted 1,4-benzodiazepin-2-one derivatives, which could be hydrolyzed under physiological conditions into certain 3-hydroxy derivatives with known pharmacological properties. These compounds comprise tertiary organic bases quaternized with 3-chloro-1,5-benzodiazepine-2-ones. Detailed investigations in the pH range 1 to 12 revealed unexpected stability of the C(3)-NR3T bond to solvolysis; formation of minor quantities of the target 3-hydroxy compounds along with strong decomposition was observed above pH 11 at room temperature. 13 references.

188256 Garrett, Edward R.; Hunt, C. Anthony. College of Pharmacy, University of Florida, Gainesville, FL 32610 **Physiochemical properties, solubility, and protein binding of delta9-tetrahydrocannabinol. (Unpublished paper).** Gainesville, Florida, University of Florida, 1973. 45 p.

The physiochemical properties, solubility and protein binding of delta9-tetrahydrocannabinol are discussed. It is contended that the rate and extent of glass binding of delta9-tetrahydrocannabinol in aqueous solution depends on the surface area and pretreatment of glass, and the concentration of drug. A method of variable plasma concentrations which was devised so that protein binding was determined from the pseudo-plasma concentrations of drug after the separation of the pseudo-plasma from the red blood cells added to form pseudo-blood with known concentrations of delta9-tetrahydrocannabinol is also discussed. (Author abstract modified)

188770 Bolt, Arthur G.; Sleigh, Merilyn J. Raymond Purves Research Laboratories, Royal North Shore Hospital, St. Leonards, N.S.W. 2065, Australia **Furoxanobenzofuroxan, a selective monoamine oxidase inhibitor.** Biochemical Pharmacology (Oxford). 23(14):1969-1977, 1974.

Furoxanobenzofuroxan (FBF), an inhibitor of monoamine oxidase, was studied. Inhibition was reversible, and of a mixed competitive and noncompetitive type. In vivo, the drug was selective in elevating the levels of indolealkylamines but not phenylethylamines. Low doses of FBF produced significant elevation of 5-hydroxytryptamine (5-HT) in the brain of the guinea pig, but not in the heart and liver. Noradrenaline (NA) levels in these organs were not affected at the low dose. An equimolar dose of tranylcypromine caused elevation of NA in the heart and brain, but had no effect on 5-HT levels. FBF was shown to be a powerful blocking agent of 5-HT in the periphery, giving it a range of properties similar to those reported for the harmala alkaloids. No evidence was found that FBF shared the hallucinogenic properties of harmine; in fact, FBF appeared to block the central action of 5-hydroxytryptophan, a known hallucinogen. The 5-HT antagonist activity of FBF appeared to predominate over its action in elevating 5-HT levels due to inhibition of monoamine oxidase. 15 references. (Author abstract)

190714 Darvas, Ferenc. EGYT Pharmacochemical Works, 1475, Budapest 10, Hungary **Application of the sequential simplex method in designing drug analogs.** Journal of Medicinal Chemistry. 17(8):799-804, 1974.

An EVOP sequential simplex optimization method is proposed for the design of drug analogs. The method is based on certain regularities in the structure of compounds having the same biological activity, and it does not require numerical calculation; the Hansch parameters and the biological activities are taken as coordiantes. The method is illustrated by retrospective examples and statistical analysis of a less favorable example indicates the method is superior to an unsystematic choice at a significance level of 0.01%. 11 references. (Author abstract modified)

190715 Shambhu, Manvendra B.; Koganty, R. Rao.; Digenis, George A. College of Pharmacy, University of Kentucky, Lexington, KY 40506 **Conformational analysis of acridan derivatives by nuclear magnetic resonance spectroscopy. A relationship between conformation and pharmacological activity.** Journal of Medicinal Chemistry. 17(8):805-809, 1974.

Six acridan derivatives with an N,N-dimethylcarboxamide group in the nine position as a common structural feature and a methyl and/or benzyl group in nine and 10 positions were synthesized and their proton magnetic resonance spectra were studied in chloroform at various temperatures. From the free energies of activation for the rotation around the CO-N amide bond and the chemical shifts of the amide methyl protons, certain conclusions were drawn regarding the conformational changes caused by the methyl and benzyl groups. With two bulky groups (amide and methyl) in the nine position, the acridan system approaches a planar time average structure. With one large group (amide) in the nine position, another large group (methyl and benzyl) in the 10 position causes the conformation of the central six membered ring to favor a highly puckered boat conformation. These results, when applied to the 9-aminoalkyl derivatives of acridan, may help to achieve a better understanding of the conformation activity relationship of the psychotropic agents related to clomacran. 19 references. (Author abstract)

190716 Borchardt, Ronald T.; Wu, Yih Shiong. Dept. of Biochemistry, University of Kansas, Lawrence, KS 66044 **Potential inhibitors of S-adenosylmethionine-dependent methyltransferases: 1. modification of the amino acid portion of S-adenosylhomocysteine.** Journal of Medicinal Chemistry. 17(8):862-868, 1974.

Structural analogs of S-adenosyl-L-homocysteine (L-SAH), with modifications of the amino acid portion of the molecule, were synthesized and their abilities to inhibit catechol O-methyltransferase, phenylethanolamine N-methyltransferase, histamine N-methyltransferase, and hydroxyindole O-methyltransferase have been investigated. The data from these inhibition studies have resulted in a delineation of the structural features of SAH which are required for enzymatic binding of this ligand. In general, it was concluded that the terminal amino group, the terminal carboxyl group, and the sulfur atom of the homocysteine portion of SAH are required for maximum binding of SAH by these enzymes. The L-configuration of the asymmetric amino acid carbon of SAH is generally required to produce maximum inhibition. The exception appears to be the potent inhibition of histamine N-methyltransferase by D-SAH.

D-SAH was substantially less effective as an inhibitor of the other enzymes tested. 24 references. (Author abstract modified)

190717 Borchardt, Ronald T.; Huber, Joan A.; Wu, Yih Shiong. Department of Biochemistry, University of Kansas, Lawrence, KS 66044 **Potential inhibitors of S-adenosylmethionine-dependent methyltransferases. 2. modification of the base portion of S-adenosylhomocysteine.** Journal of Medicinal Chemistry. 17(8):868-873, 1974.

The specificity of S-adenosyl-L-homocysteine (SAH) inhibition of enzymatic transmethylation was explored by preparing structural analogs of SAH in which the base portion of the molecule was modified. The various SAH analogs were evaluated as inhibitors of catechol O-methyltransferase, phenylethanolamine N-methyltransferase, histamine N-methyltransferase, and hydroxyindole O-methyltransferase. Inhibition studies indicate that there exists a specificity by these enzymes for the adenine portion of SAH, with an absolute requirement of the six amino group for maximum activity. Substitution of other pyrimidine and purine bases in place of adenine resulted in complete loss of activity. However, minor modifications of the adenine moiety of SAH could be tolerated at the enzymatic binding sites. For example, S-3-deazaadenoysl-L-homocysteine had inhibitory activity similar to that SAH itself. Some differences in the binding requirements of these methyltransferases have been observed so that differential inhibition may be possible. 26 references. (Author abstract)

191498 Shih, Jean C.; Eiduson, Samuel. Neuropsychiatric and Brain Research Institutes, Medical School, University of California at Los Angeles, Los Angeles, CA **Some interrelated properties of brain monoamine oxidase.** Psychopharmacology Bulletin. 10(3):7-8, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, some interrelated properties of brain monoamine oxidase (MAO) were reported, as determined by analysis via fractionation using chromatography or Sephadex electrophoresis (SE). The previous research finding of two major protein peaks (A and B) when the enzyme was separated by agarose column chromatography was further analyzed. Findings included the observation that there are multiple forms of MAO in one fractionation; that the various forms may be interdependent and concentration dependent; and that perhaps one form of regulation of the turnover of the biogenic amines might be the interconversion of the different forms with different substrate affinities. 1 reference.

191499 Martin, Yvonne C.; Biel, John H. Abbott Laboratories, North Chicago, IL **Some considerations in the design of substrate and tissue specific inhibitors of MAO.** Psychopharmacology Bulletin. 10(3):8-9, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the design of monoamine oxidase (MAO) inhibitors that do not penetrate the brain was discussed using substituted beta-carbolines as an example. In one experiment, the potency and lack of CNS effect of 2,9-dimethylcarbolinium iodide were demonstrated. The inhibition of serotonin oxidation of pargyline analogs was evaluated by regression analysis and results indicate that electronic effects predominate in the structure - activity relationships of parygyline analogs, with steric effects being next in importance. The potentiation of the DOPA response in mice by substituted 1-amino-indanes and 1-aminotetralines was studied by discriminant analysis and steric and electronic effects again predominated. Overall, findings suggest that quantitative structure - activity studies can provide guides to synthesis of new analogs which are especially useful when several biological properties of the molecules have been correlated with physical properties. In such instances an optimization of desirable versus undesirable activities can be suggested. 6 references.

191523 Roffman, M.; Riegle, T.; Orsulak, P.; Schildkraut, J. J. Harvard Medical School, Boston, MA **Comparative properties of soluble and particulate catechol-O-methyl transferase from rat red blood cell: preliminary observations.** Psychopharmacology Bulletin. 10(3):43, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, preliminary observations were reported on the comparative properties of soluble and particulate catechol-O-methyl transferase (COMT) from rat red blood cells. The ultimate aim was to examine the properties of COMT enzymes in red blood cells in patients with psychiatric illnesses, including the affective, schizophrenic, and addictive disorders. Results confirm the earlier findings that two COMT's (free and bound forms) differing in several physical and chemical properties exist within the rat red blood cells. The human red blood cell is now being examined in an effort to identify a comparable membrane bound COMT. 2 references.

192878 Crosby, D. M.; McLaughlin, J. L. Dept. of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **Cactus alkaloids. XIX. Crystallization of mescaline HCl and 3-methoxytyramine HCl from Trichocereus pachanoi.** Lloydia. 36(4):416-418, 1973.

The cactus Trichocereus pachanoi was investigated to determine whether the mescaline contents of these plants is sufficient to make the species a serious item of drug abuse. Trace alkaloids were also crystallized to confirm their presence. Mescaline base was isolated from freeze dried plant material. The major phenolic alkaloid, 3-methoxytyramine HCl was isolated and crystallized utilizing preparative thin layer chromatography. This is apparently the first report of the crystallization of 3-methoxytyramine from the plant kingdom, and the small concentration found in the plant is likely insufficient to cause any effects upon ingestion of preparations made from the plant material. 20 references.

192879 Dingerdissen, J. J.; McLaughlin, J. L. Dept. of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue University, West Lafayette, IN 47907 **Cactus alkaloids. XXII. Dolichothele surculosa and other Dolichothele species.** Lloydia. 36(4):419-421, 1973.

It was concluded from chromatographic screening of five members of the cactus genus Dolichothele that the genus is rich in alkaloids. D. surculosa, a species native to Tamaulipas, Mexico was found to contain four major alkaloids (N-methylphenethylamine, N-methyltyramine, synephrine, and hordenine) which were isolated and crystallized as their hydrochlorides. The detection of dolichotheline and unknown alkaloids in other Dolichothele species and the isolation of beta-phenethylamines from D. sphaerica and D. surculosa contributes to chemotaxonomy and supports the classification of this genus as separated from the genus Mammillaria. The presence of the sympathomimetic beta-phenethylamine alkaloids confers explainable physiological activity on D. surculosa. 16 references.

192882 West, L. G.; McLaughlin, J. L. Dept. of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue Univ., West Lafayette, IN 47907 **Cactus alkaloids: XVIII. Phenolic beta-phenethylamines from Mammillaria elongata.** Lloydia. 36(3):346-348, 1973.

Thin layer chromatographic (tlc) examination of alkaloid extracts of Mammillaria elongata De Candolle, a species of cactus native to eastern Mexico, was made. The examination revealed traces of five alkaloids. No alkaloids were detected in the nonphenolic fractions. Using preparative tlc, small quantities of the crystalline hydrochlorides of two of the alkaloids were isolated. Attempts to crystallize the small amounts of the remaining three alkaloids were unsuccessful but they were identified as tyramine, N-methyltyramine and beta-O-methylsynephrine. Preparation and identification procedures are described. 15 references.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

189023 Froment, Jean-Louis; Petitjean, Francoise; Bertrand, Nicole; Cointy, Colette; Jouvet, Michel. Departement de Medecine Experimentale, Universite Claude-Bernard, 8, avenue Rockefeller, 69373 Lyon Cedex 2, France /**Effects of intracerebral injection of 5,6-hydroxytryptamine on cerebral monoamines and sleep states in the cat/.** Effets de l'injection intracerbrale de 5,6-hydroxytryptamine sur les monoamines cerebrales et les etats de sommeil du chat. Brain Research (Amsterdam). 67(3):405-417, 1974.

The effects of intracerebral injection of 5,6-hydroxytryptamine (5,6-HT) on cerebral monoamines and sleep waking cycle of the cat were studied. The sleep waking cycle was recorded continously in 29 chronically implanted cats for 15 days after the intraventricular or intracerebral (in the rostral part of the raphe system) injection of 5,6-HT. The intraventricular injection of 1mg of 5,6-HT induced a secondary and important decrease of 5-HT and 5-hydroxyindoleacetic acid (5-HIAA) at the cortical and subcortical levels. Neither noradrenaline nor dopamine endogenous levels were significantly altered. The intraventricular injection of 5,6-HT immediately induced a state of sedation accompanied by cortical activation. The injection of 13mg of 5,6-HT directly into the rostral part of the raphe system did not induce any significant alterations of cerebral monoamines. The results are in accordance with the monoaminergic theory of sleep. 22 references. (Author abstract modified)

189177 Borgman, Robert J.; Baylor, Michael R.; McPhillips, Joseph J.; Stitzel, Robert E. Division of Medicinal Chemistry, School of Pharmacy, West Virginia University, Morgantown, WV 26505 **Alpha-methyldopamine derivatives. Synthesis and pharmacology.** Journal of Medicinal Chemistry. 17(4):427-430, 1974.

Several labile, lipophilic analogs of alpha-methyldopamine were synthesized and evaluated pharmacologically for dopamine receptor activation and potential anti-Parkinson activity. The compounds were synthesized by selective O-acetylation and N-alkylation procedures. The activity of the compounds was examined in each of three animal experimental models, which included protection against oxotremorine induced tremor in mice, antagonism of both reserpine induced motor depression and ptosis in mice, and production of hypothermia in mice and its antagonism by haloperidol. Compound 10 showed dopamine receptor stimulating properties and was able to antagonize oxotremorine induced inhibition of motor activity. Findings are consistent with a previous suggestion that O-acetylation and N-alkylation are required to confer activity in some tests which have been proposed for evaluating dopaminergic and/or anti-Parkinson activity. 21 references. (Author abstract modified)

189178 Walter, Lewis A.; Chang, Wei K.; Kenney, Joanne; Douvan, Irina. Medicinal Chemistry Research Department, Schering Corporation, Bloomfield, NJ 07003 **Synthesis and central nervous system activity of 1,2,3,4-tetrahydro-1-amino-4-phenylnaphthalenes.** Journal of Medicinal Chemistry. 17(4):459-463, 1974.

The synthesis and central nervous system activity of 1,2,3,4-tetrahydro-1-amino-4-phenylnaphthalenes are reported. Subjects were mice who were treated orally or intraperitoneally with varying dosage schedules of the compounds. With most pairs of the isomeric amines, the isomers with the x configuration were more behaviorally active as stimulants and more toxic than their y counterparts; the latter were more active as depressants. Although not administered by the same route, two pairs are an apparent exception. Only two pairs showed any analgetic action, and this only at doses 30 and 10 times greater, respectively, than those producing depression. 14 references.

189584 Lahti, Robert A.; Lednicer, Daniel. Research Laboratories, Upjohn Company, Kalamazoo, MI 49001 **Effect of a butyrophenone derivative, U-32,802A, on brain biogenic amines.** Biochemical Pharmacology (Oxford). 23(12):1701-1705, 1974.

The effect of a butyrophenone derivative, U-32802A, on brain biogenic amines was examined in mice. U-32802A was found to block the uptake of and to cause a release of 3H-norepinephrine from the mouse heart. The releasing effect of U-32802A was not blocked by pretreatment with protriptyline at 10mg/kg. U-32802A caused a severe and long-lasting depletion of mouse brain norepinephrine and dopamine with little effect on serotonin at a dose of 5mg/kg. U-32802A also caused an increase in homovanillic acid in mouse striatum a property common to a variety of antipsychotic agents. The spectrum of activity of U-32802A is different from that of either haloperidol or reserpine and may represent a new class of amine depleting agents. 8 references. (Author abstract)

190719 Nelson, Wendell L.; Sherwood, Bob E. School of Pharmacy, University of Washington, Seattle, WA 98195 **Centrally acting muscle relaxants. Isomeric 9,10-dihydroxy-1,2,3,4,4a,9,10,10a(trans-4a,10a)-octahydroph henanthrenes and their carbamate esters.** Journal of Medicinal Chemistry. 17(8):904-907, 1974.

The isomeric 9,10-dihydroxy-1,2,3,4,4a,9,10,10a(trans-4a,10a)-octahydrophenanthrene and their carbamate esters were prepared and screened for anticonvulsant activity in a study of conformational aspects of activities of muscle relaxant diols and carbamate esters. Data show some muscle relaxant effects for the diols as demonstrated by the protection against pentylene-tetrazole. Preliminary results suggest some central depressant effects of the diols similar to the muscle relaxant tranquilizer mephenesin or meprobamate. The difference in activity of the individual diols may be related to differences in distribution or metabolism and not necessarily related to a drug receptor interaction. 16 references.

191783 Allikmets, L. Kh. Central Medical Scientific-Research Laboratory, Tartu University /**Correlation between the tranquilizing and sedative action of neuroleptics, antidepressants and anticholinergic drugs.**/ Sootnosheniye mezhdu trankviliziruyushchim i sedativnym deystviyem v ryadu neyroleptikov, antidepressantov i antikholinergicheskikh veshchestv.

In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 78-85). Vol. 9.

The tranquilizing and sedative effects of 21 psychotropic and anticholinergic drugs were compared. Tranquilizing effects were measured by suppression of squeaking and fighting produced by electric current in albino rats; the sedative effects were measured by suppression of exploratory motor activity. The tranquilizing and sedative effects of the neuroleptics promazine, chlorpromazine, acepromazine, haloperidol and triperidol were in positive correlation. The tranquilizing effects considerably exceeded the sedative effects of the neuroleptics levomepromazine, chlorprothixene, and fluphenazine. The neuroleptics trifluoperazine, perfenazine, prochlorperazine and thioproperazine exerted strong sedative but no tranquilizing action. Among antidepressants only amitriptyline and nortriptyline had weak tranquilizing action. 26 references. (Author abstract modified)

191784 Mekhilane, L. S. Laboratory of Psychopharmacology Tartu University, Tartu, USSR /**Neurochemical analysis of aggressive - defensive behavior elicited by electrical stimulation of the hypothalamus and central gray matter.**/ Neyrokhimicheskiy analiz agressivno-oboronitel'nogo povedeniya, vyzvannogo elektrorazdrazheniyem gipotalamusa i tsentral'nogo serogo veshchestva. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 86-97). Vol. 9.

The effects of electrical stimulation of various parts of the hypothalamus and central gray matter of cats were studied. Stimulation of the central lateral part of the hypothalamus and central gray matter elicited affective vocalizations and flight response. Stimulation of the central medial and posterior hypothalamic regions elicited attack behavior with affective vocalizations. Instramuscular injection of physostigmine intensified or lowered the threshold of benactyzine and amphetamine antagonized or increased the threshold of emotional reactions elicited by electrical stimulation of the anterior hypothalamus. Physostigmine and amphetamine intensified the reactions caused by stimulation of the posterior hypothalamus and mesencephalon. 28 references. (Author abstract modified)

191785 Allikmets, L. Kh.; Mekhilane, L. S. Central Medical Scientific-Research Laboratory, Tartu University, Tartu, USSR /**The action of levomepromazine and trimeprimine on effector centers of emotions in the hypothalamus.**/ Deystviye levomepromazina i trimeprimina na effektornyye tsentry emotsii v gipotalamuse. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 98-108). Vol. 9.

The relationship between the sedative and tranquilizing effects of levomepromazine and trimeprimine, on one hand, and other psychopharmacological substances, on the other, was examined. Behavioral activation and emotional reactions were stimulated in cats by means of electrodes implanted in the hypothalamic region. Levomepromazine was found to be much stronger in suppressing orienting response, but trimeprimine was more effective in inhibiting emotional reactions. Benactyzine and amphetamine increased the tranquilizing effect of levomepromazine and trimeprimine. Physostigmine was antagonistic to both the sedative and tranquilizing effects of levomepromazine and trimeprimine. 34 references. (Author abstract modified)

191786 Mekhilane, L. S.; Vakhing, V. A. Central Medical Scientific Research Laboratory, Tartu University, Tartu, USSR /**Influence of levomepromazine and trimeprimine on effects of electrical stimulation and microinjection of acetylcholine, serotonin and noradrenaline into the mesencephalon.**/ Vliyaniye levomepromazina i trimeprimina na effekty elektrorazdrazheniya i mikroin'ektsii atsetilkholina, serotonina i noradrenalina v sredniy mozg. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 109-117). Vol. 9.

The effects of levomepromazine and trimeprimine on activity, affective, and visceral reactions of cats were studied. Levomepromazine and trimeprimine were equal in suppressing aggressiveness elicited by electrical stimulation of the mesencephalon. Levomepromazine was more effective in inhibiting exploratory motor reaction and cholinergic aggressiveness. Benactyzine and amphetamine increased and physostigmine weakened the tranquilizing action of levomepromazine. In small doses (0.3-1.0mg/kg IM) levomepromazine and trimeprimine increased the behavioral and visceral reactions elicited by the intramesencephalic injection of noradrenaline and serotonin. 27 references. (Author abstract modified)

191787 Karu, L. E. Central Medical Scientific Research Laboratory, Tartu University, Tartu, USSR /**Action of haloperidol and trifluoperazine on the motor responses elicited by electrical stimulation of the brain in rabbits.**/ Deystviye galoperidola i trifluoperazina na dvigatel'nyye proyavleniya, vyzvannyye elektrorazdrazheniyem struktur mozga u krolikov. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (P. 118-128). Vol. 9.

The effects of haloperidol and trifluoperazine on motor and behavioral responses elicited by electrical stimulation of the caudate, ventrolateral thalamic nuclei and midbrain reticular formation of rabbits were studied. Both neuroleptics inhibited the selected components of orienting reflex in all structures to a similar extent. Haloperidol was more effective in inhibiting certain somatomotor responses than was trifluoperazine. Some motor components were more sensitive to inhibition; they included contraversive turn of the head, flexion of contralateral foreleg, ipsilateral rotation of the head, and ipsiversive circling movements in reticular stimulation. Others, including mastication, upward movement of the head in caudate stimulation, increased muscle tone, ipsiversive twisting of the trunk in ventrolateral thalamic stimulation, and increased muscle tone in reticular stimulation, were resistant. 22 references. (Author abstract modified)

191900 Eberts, Floyd S., Jr. Upjohn Company, Kalamazoo, MI 49001 **Comparative metabolism of triazolam, a new sedative-hypnotic, in rat, dog and man.** Pharmacologist. 16(2):196, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, triazolam (I), 8-chloro-6-(o-chlorophenyl)-l-methyl-4M-s-triazolo04,3-a0
01,40benzodiazepine, a new potent, shortacting, sedative hypnotic drug with a novel triazolobenzodiazephine structure was examined. When 14C-labeled I was administered orally to male rats, dogs, and humans, the distribution of recovered 14C was as follows: urine -- 16% (R), 43% (D), 91% (H); feces -- 84% (R), 53% (D), 9% (H). Pooled urine from each species was examined for metabolites. Evidence was found for small amounts of unmetabolized I in all species, plus 12 metabolites in rats, 10 metabolites in dogs, and 6 metabolites in man. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

187362 Dafny, Nachum; Gilman, Sid. Neurobiology, University of Texas Medical School, Houston, TX 77025 **Alteration of evoked potentials in caudate nucleus of freely moving rats by L-dopa, reserpine, and pentobarbital.** Experimental Neurology. 42(1):51-64, 1974.

The alteration of evoked potentials in caudate nucleus of freely moving rats by L-dopa, reserpine, and pentobarbital is reported. Average acoustic responses were recorded with permanent semi-microelectrodes from the caudate nucleus in freely behaving rats. Administration of pentobarbital enhanced the amplitude of the responses and shortened the neuronal recovery function. Higher doses of pentobarbital progressively diminished the amplitude of the responses. L-dopa increased the amplitude of the average acoustic evoked responses and shortened the neuronal recovery function when paired acoustic stimuli were delivered at varied interstimulus intervals. Reserpine administration 1 hr after L-dopa injection reversed these phenomena, producing a decrease of the responses and prolongation of the neuronal recovery function. When administered as the first treatment, reserpine reduced the amplitude of the responses, but shortened the neuronal recovery function. L-dopa injection after reserpine treatment reversed the reserpine effect, i.e.,increased the amplitude of the responses and shortened further the neuronal recovery function. It is concluded that L-dopa intensifies and reserpine diminishes neuronal evoked responses within caudate nucleus, presumably by altering the activity of neurotransmitters. 26 references. (Author abstract)

187380 Richardson, J. Steven; Cowan, Nelson; Hartman, Rebecca; Jacobowitz, David M. Dept. of Pharmacology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada **On the behavioral and neurochemical actions of 6-hydroxydopa and 5,6-dihydroxytryptamine in rats.** Research Communications in Chemical Pathology and Pharmacology. 8(1):29-44, 1974.

Intraventricular injection of neurotoxic agents 6-hydroxydopa and 5,6-dihydroxytryptamine and subsequent chemical behavior in rats is reported. When injected intraventricularly, 90mg of 6-hydroxydopa reduces consumatory and locomotor behaviors, and increases emotionality. The deficits in food and water consumption may be due to the reduction of brain norepinephrine levels which disrupts the balance between the noradrenergic and the dopaminergic neurotransmitter systems. The reduced open field locomotion is correlated with an absolute increase in brain serotonin levels that occurs during the few days just after the injection of 6-hydroxydopa. The increased emotionality might be due to a relative predominance of serotonin in the norepinephrine - serotonin balance that underlies emotional tone. 11 references. (Journal abstract modified)

187381 Zabik, Joseph E.; Van Dam, David P.; Maickel, Roger P. Department of Pharmacology, Medical Sciences Program, Indiana University, Bloomington, IN 47401 **Pharmacological and toxicological studies on 1,4-butanediol.** Research Communications in Chemical Pathology and Pharmacology. 8(1):83-90, 1974.

Preliminary pharmacological data concerning spontaneous motor activity and reflex action in rats administered doses 1,4-butanediol (1,4-BD) daily for 2 weeks is reported. 1,4-Butanediol had a significant sedative effect on rats at i.p. dosages 300mg/kg. The LD50 was 1328 mg/kg. Effects of the drug on spontaneous motor activity was biphasic; doses of 50-200mg/kg significantly reduced activity, while doses of 300-400mg/kg produced loss of righting reflex. No increase in livertriglycerides was seen even at doses of 1000mg/kg/day for 14 days. It is concluded that 1,4-BD is a unique sedative drug, quite dissimilar to ethanol. 13 references. (Journal abstract modified)

187397 Thoa, Nguyen B.; Wooten, G. Frederick; Axelrod, Julius; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **On the mechanism of release of norepinephrine from sympathetic nerves induced by depolarizing agents and sympathomimetic drugs.** (Unpublished paper). Bethesda, MD, NIMH, 1974. 11 p.

The effect of depolarizing agents on release of norpinephrine (NE) was investigated in guinea pig vasa deferentia in vitro. Depolarization by either hypertonic potassium chloride or veratridine resulted in a dose dependent, proportional release of NE and dopamine-beta-hydroxylase (DBH). Exocytosis from sympathetic nerve terminals may be elicited by depolarizing drugs as well as by electrical stimulation. Incubation in the presence of reserpine or tyramine, d-amphetamine, or metaraminol resulted in the dose dependent release of NE but not DBH. Findings indicate that tyramine may act by displacing NE from cytoplasmic stores into the synaptic space. Release by exocytosis may occur in the presence of a depleted amine store, and the NE released by exocytosis may be derived predominantly from vesicular reserpine sensitive stores. 29 references. (Author abstract modified)

187496 Freedman, Robert; Hoffer, B. J.; Siggins, G. R. St. Elizabeths Hospital, Wm. A. White Bldg., Washington, DC 20032 **Neuroleptic antagonism of catecholamine inhibitions in rat cerebellum and caudate.** (Unpublished paper). Washington, DC, NIMH, 1974. 1 p.

The neuroleptics fluphenazine (FPZ) and flupenthixol (FPT) were tested against two model central catecholamine systems -- the noradrenergic inhibition of Purkinje neurons in rat cerebellum arising from locus coeruleus and the dopaminergic inhibition of caudate neurons arising from substantia nigra -- in order to test the theory that neuroleptics exert clinical and behavioral effects by interaction with brain monoamine pathways. Iontophoresis of cyclic AMP produced inhibitions in both neural systems, which were not antagonized by neuroleptics. This finding is compatable with biochemical evidence that therapeutic neuroleptics can block catecholamine stimulation of adenyl cyclase and suggests that this action may underlie the behavioral effects. (Author abstract modified)

187526 Trabucchi, M.; Cheney, D. L.; Racagni, G.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Pentobarbital and in vivo turnover rate of acetylcholine in mouse brain and in regions of rat brain.** (Unpublished paper). Washington, D.C., NIMH, 1974. 14 p.

The in vivo turnover rate of acetylcholine (ACh) was measured in the total brain of mice and brain parts of rats after treatment with sodium pentobarbital (Na-PB), parachlorophenylalanine (CPA) and following REM sleep deprivation for 96 h. Na-PB decreased the turnover rate of ACh both in total brain of mice and in cortex of rats but no significant changes were detected in the striatum. Subchronic treatment with para-CPA decreased the cortical content of ACh and choline and partially reversed the decrease of turnover rate of ACh elicited by Na-PB. In REM sleep deprived rats the turnover rate of ACh in the cortex was increased. 27 references. (Author abstract)

187527 Costa, E.; Trabucchi, M. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Regulation of brain dopamine turnover rate: pharmacological implications. (Unpublished paper).** Washington, DC, NIMH, 1974, 57 p.

The theoretical and technical difficulties faced when the dopaminergic neurons are studied in vivo to detect how drugs and environment affect their function are discussed. The discussion is concerned with: problems in interpreting the compartmentation and the functional implications of turnover rate measurements of neuronal dopamine (DA); molecular mechanisms for the regulation of dopaminergic neurons; and interaction of the nigrostriatal dopaminergic systems with other neuronal systems. A hypothetical model is proposed to interpret how various drugs modify the function of striatal dopaminergic synapses. Various drugs (DA, apomorphine or amphetamine) are seen as acting either at the postsynaptic or at the presynaptic parts of DA nerve terminals. Results are fully discussed and predictions are made concerning the effects of neuroleptics. 72 references. (Author abstract modified)

187552 Vaquez, A. J.; Krip, G. Chicago Medical School, Chicago, IL 60612 **Evidence for an inhibitory role for acetylcholine, catecholamines, and serotonin on the cerebral cortex.** In: Modulators in cortical slabs. New York, Raven Press, 1973. (p. 137-159).

The electrical phenomena in response to direct stimulation of a limited population of cortical neurons was studied in cats subsequent to the administration of some of the mediators and modulators known to be operative in cortical neurons, namely acetylcholine (ACh), catecholamines and serotonin (5-HT). Pharmacological agonists and antagonists of these mediators were administered in unanesthetized and unrestrained animals with neuronally isolated chronic cortical slabs. Studies were made on the effects of cholinergic drugs and their antagonists on epileptiform afterdischarges; the effects of adrenergic agents and their antagonists on epileptiform afterdischarges; the effects of 5-HT agonists and antagonists on afterdischarge duration; and the interactions between cholinergic and monoaminergic mechanisms in the modulation of the epileptiform afterdischarges. Results indicated that it is not possible to show an excitatory action for any of the central neurohumoral candidates investigated, ACH, 5-HT and noradrenaline. 76 references.

187573 Buyniski, J. P.; Smith, M. L.; Bierwagen, M. E. Pharmacology Department, Bristol Laboratories, Syracuse, NY 13201 **Cardiovascular and gross behavioral effects of amphetamine, 2-amino-1-(2,5-dimethoxy-4-methylphenyl) propane (DOM) and 2-amino-1-(2,5-dimethoxy-4-methylphenyl) butane (BL-3912A) in the conscious dog.** Research Communications in Chemical Pathology and Pharmacology. 8(2):213-221, 1974.

The behavioral and cardiovascular effects of amphetamine, 2-amino-1-(2,5-dimethoxy-4-methylphenyl) propane (DOM) and 2-amino-1-(2,5-dimethoxy-4-methylphenyl) butane (BL-3912A) were observed in conscious dogs and found to result in appreciable gross behavioral and cardiovascular changes. Behavioral changes ranged from stereotyped activity and disorientation with amphetamine to catatonia with DOM and brief central nervous system stimulation with BL-3912A. In conscious dogs, all three drugs raised mean aortic blood pressures with amphetamine being the most effective, followed by DOM and BL-3912A. Heartrate was consistently reduced only by amphetamine. BL-3912A resulted in depressor responses on blood pressure in anesthetized dogs, suggesting that in the conscious dog, the drug may be activating centers in the central nervous system to effect a pressor response. The elevation of blood pressure in the conscious dog induced by amphetamine and DOM is mediated, at least partly, via their peripheral actions. 8 references. (Author abstract modified)

187576 Narasimhachari, N.; Lin, R.-L. Thudichum Psychiatric Research Laboratory, Galesburg State Research Hospital, Galesburg, IL 61401 **A possible mechanism for the antischizophrenic action of chlorpromazine: inhibition of the formation of dimethyltryptamine by chlorpromazine metabolites.** Research Communications in Chemical Pathology and Pharmacology. 8(2):341-351, 1974.

The use of mono-N-demethyl-chlorpromazine (nor1CPZ) di-N-demethylchlorpromazine (nor2CPZ), two key N-demethylated metabolites of chlorpromazine, were investigated as substrates for the enzyme indolethylamine N-methyltransferase. Both were found to be good substrates. The Km values are lower and substrate affinities are higher than those for tryptamine compounds. At equimolar concentrations, nor1CPZ and nor2CPZ exert inhibitory effects on the N-methylation of N-methylserotonin and N-methyltryptamine. A possible role for these metabolites in the antischizophrenic (antipsychotic) activity of chlorpromazine is postulated. 18 references. (Author abstract modified)

187578 Estevez, Vicente S.; Englert, Leo F.; Ho, Beng T. Texas Research Institute of Mental Sciences, Houston, TX 77025 **Effect of SKF-525-A on the metabolism of (-)-delta9-tetrahydrocannabinol in the rat brain and liver.** Research Communications in Chemical Pathology and Pharmacology. 8(2):389-392, 1974.

The metabolism of delta9-tetrahydrocannabinol (THC) in rats under the influence of SKF-525-A was investigated, and pretreatment with SKF-525-A resulted in nearly 50% decrease of 11-OH-delta9-THC in both the brain and liver, as compared with animals without pretreatment. The microsomal oxidation inhibitor also caused a reduction of the dihydroxylated metabolites, 8,11-(OH)2-delta9-THC, to 14% of control values. The large reduction of the acid metabolite in the brain (65% of control) and the liver (16% of control) by SKF-525-A indicates the oxidative pathway producing the acid is a microsomal process. 5 references. (Author abstract modified)

187645 Koyuncuoglu, Hikmet. Dept. of Pharmacology, Istanbul Medical Faculty of Istanbul University, Istanbul, Turkey **The effects of chronic reserpine and nialamide treatment on the free amino acid levels of rat brain.** Psychopharmacologia (Berlin). 37(1):87-90, 1974.

The opposing effects of reserpine and nialamide on brain catecholamine content were reflected in changes in brain tyrosine level. The effects of nialamide may be due directly to increased levels of aspartic and glutamic acids which excite central neurons. 8 references. (Author abstract modified).

187677 Organisciak, D. T.; Klingman, J. D. Neurosensory Laboratory, Dept. of Physiology, State University of New York, 2211 Main St., Buffalo, NY 14214 **The effects of lithium on high energy phosphate and glucose levels in the rat superior cervical ganglion.** Journal of Neurochemistry (Oxford). 22(3):341-345, 1974.

The effects of acute treatment with lithium ion (25 mM) on the levels of ATP, phosphocreatine and glucose were measured in an in vivo preparation of rat superior cervical ganglion. Similar analyses were performed on ganglia from rats

fed a chronic lithium diet (0.5mM). Ganglia were excised and desheathed, then stimulated (5 Hz) or rested for 20, 40 or 80 min in normal or lithium containing Krebs-Ringer bathing solutions. Following freeze drying, enzymatic pyridine nucleotide methods were used to measure fluorometrically ATP, phosphocreatine and glucose on portions of a ganglionic perchloric acid extract. After 20 min of incubation, normal ganglionic contents of ATP and phosphocreatine were higher than the initial zero time levels. Incubation for periods longer than 20 min resulted in ATP and phosphocreatine levels which were lower than those at zero time. Stimulation of normal ganglia caused a decrease in the contents of high energy phosphates relative to those in the resting state. Except for the 20 min time period the ATP levels were lower than normal in ganglia from rats chronically fed lithium. Levels of ATP and phosphocreatine in ganglia acutely exposed to lithium were significantly lower than in both normal ganglia and ganglia from chronically treated rats. In comparison to normal ganglia, significantly lower levels of glucose were found only for stimulated ganglia acutely exposed to lithium. 32 references. (Author abstract)

187695 Stricker, Edward M.; Zigmond, Michael J. Psychobiology Program, Dept. of Psychology, Univ. of Pittsburgh, Pittsburgh, PA 15260 **Effects on homeostasis of intraventricular injections of 6-hydroxydopamine in rats.** Journal of Comparative & Physiological Psychology. 86(6):973-994, 1974.

The effects on homeostasis of intraventricular injections of 6-hydroxydopamine (6-HDA) were studied in the rat. Intraventricular injections of 6-HDA after pretreatment with desmethylimipramine and pargyline, or pargyline alone, produced severe depletions of brain dopamine (DA) in rats. Animals became aphagic and adipsic, showed prolonged periods of anorexia before again accepting dry chow and water, maintained low bodyweights, did not increase food intakes after injections of 2-deoxy-D-glucose and delayed drinking to thirst stimuli. Rats did not have impairments of feeding efficiency, learned taste aversions, or thermoregulation during heat stress. Results suggest that brain catecholamines play an important role in some regulatory processes but that lateral hypothalamic lesions may not be tantamount to destruction of the DA containing neurons of the nigrostriatal pathway. 120 references. (Author abstract modified)

187799 LeBlanc, J.; Cote, J.; Dore, F. Department of Physiology, School of Medicine, Laval University, Quebec, Quebec **Effects of guanethidine and imidazole on histamine response.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):483-488, 1974.

The effects of an alpha blocker and of noradrenaline on the actions of both guanethidine and imidazole on histamine release were studied in rats by blood pressure response. Guanethidine was shown to increase sensitivity not only to noradrenaline but to acetylcholine and histamine. This effect of guanethidine on histamine is not likely explained by lack of reflex sympathetic activity resulting from chronic treatment but possibly by a reduced uptake of histamine. Similarly, chronic treatment with guanethidine, by increasing histamine release, could have increased tolerance to histamine, thus explaining some of the results obtained. This is not the case since chronic treatment with histamine was shown to increase rather than decrease response to histamine in the rat. Imidazole did not potentiate histamine, noradrenaline, or acetylcholine response and possesses some slight antihistaminic effect. Finally, noradrenaline blocks the effect of guanethidine on release of histamine but has no effect on the action of imidazole. 11 references. (Author abstract modified)

187800 Bhatnagar, Satya P. Drug Research Laboratories, Health Protection Branch, Dept. of National Health and Welfare, Tunney's Pasture, Ottawa K1A 0L2 **Actions of atropine, hemicholinium-3, and physostigmine on chlorpromazine-induced changes in rat brain monoamines.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):500-507, 1974.

The influence of atropine, hemicholinium-3 (HC-3), and physostigmine on the accumulation of monoamines after monoamine oxidase inhibition with pargyline, and on their disappearance after synthesis inhibition with alpha-methyl-p-tyrosine (alpha-MT) was investigated in whole brain of normal and chlorpromazine (CPZ) treated rats. The accumulation of dopamine (DA) and serotonin (5-HT) is significantly inhibited by atropine and HC-3, as is the loss of DA. Only HC-3 affected the noradrenaline (NA) accumulation. Both atropine and HC-3 increased while physostigmine inhibited the disappearance of NA, but had no effect on the normal cerebral concentrations of monoamines. CPZ increased the accumulation of DA and 5-HT and the loss of DA and NA without affecting their normal concentrations. HC-3 atropine inhibited the action of CPZ on the accumulation of DA and 5-HT, and inhibited the CPZ induced accentuation of DA loss but enhanced that of NA. Physostigmine produced the opposite effects. Results support the hypothesis of cholinergic - aminergic interaction at the cerebral level and demonstrate the usefulness of HC-3 as a tool in such investigations. 37 references. (Author abstract modified)

187801 Seeman, P.; Lee, T. Pharmacology Department, University of Toronto, Toronto, Ontario M5S 1A8 **Enhanced binding of chlorpromazine to cholesterol-depleted synaptosome fractions.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):522-525, 1974.

Brain synaptosome fractions were treated by Murphy's method in order to deplete the membrane cholesterol, and the binding of 35S-chlorpromazine to these treated membranes was measured. It was found that the membrane buffer partition coefficient of the drug was threefold greater in the treated synaptosome rich fractions compared with the untreated fractions. The results suggest that cholesterol may not be a part of the membrane hydrophobic binding site for tranquilizers. 35 references. (Author abstract modified)

187802 Seeman, P.; Chen, S. S.; Chau-Wong, M.; Staiman, A. Department of Pharmacology, University of Toronto, Toronto, Ontario M5S 1A8 **Calcium reversal of nerve blockade by alcohols, anesthetics, tranquilizers, and barbiturates.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):526-534, 1974.

The results of a study of calcium (Ca2+) reversal of rat phrenic nerve blockage by alcohols, anesthetics, tranquilizers, and barbiturates are presented. Results show that Ca2+ reversed the nerve blocking actions of procaine, lidocaine, procainamide, imipramine, chlorpromazine, tetrodotoxin, hexanol, heptanol, benzyl alcohol, thymol, sodium barbital, and sodium pentobarbital. An elevation of external Ca2+ restored the blocked compound action potential of the nerve for all three types of drugs: cationic, anionic, and uncharged. The data do not support the idea that Ca2+ and drugs compete for membrane binding sites, and it is concluded that Ca2+ may cause a physiological kind of allosteric antagonism of the drug blocked sodium (Na+) channel, or a direct augmentation of the Na+ conductance. 31 references. (Author abstract modified)

187803 Staiman, A.; Seeman, P. Dept. of Pharmacology, Univ. of Toronto, Toronto, Ontario, M5S 1A8 **The impulse-blocking concentrations of anesthetics, alcohols, anticonvulsants, barbiturates, and narcotics on phrenic and sciatic nerves.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):535-550, 1974.

The fiber size dependence of the nerve blocking concentrations of drugs was studied using: two types of myelinated nerves (rat phrenic and sciatic), the same myelinated nerve at different states in growth, a variety of nerve blocking drugs (anesthetics, alcohols, tranquilizers, antidepressants, anticonvulsants, barbiturates, and narcotics), Skau's method of equilibrium blockage, and many concentrations to obtain a full dose response curve. The results show that whether different nerves or the same nerve at different stages of growth are compared, smaller myelinated fibers require lower nerve blocking concentrations of drugs. 52 references. (Author abstract modified)

187804 Muller, P.; Seeman, P.; Spero, L. Department of Pharmacology, University of Toronto, Toronto, Ontario M5S 1A8 **The additive effects of tranquilizers and dopamine on smooth muscle.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):551-557, 1974.

The effects of the tranquilizers chlorpromazine and haloperidol on smooth muscle response to dopamine were studied to test the receptor blockade theory. The results do not support the receptor blockade theory of neuroleptic action since the neuroleptic and dopamine actions in the ileum were additive. The evidence provides some support for the excitability blockade hypothesis of neuroleptic action. 32 references. (Author abstract modified)

187806 Phillis, J. W.; Limacher, J. J. Department of Physiology, College of Medicine, Univ. of Saskatchewan, Saskatoon, Saskatchewan S7N OWO **Effects of some metallic cations on cerebral cortical neurones and their interactions with biogenic amines.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):566-574, 1974.

The interrelationship among the actions of calcium, the biogenic amines, various metallic cations used as calcium antagonists (cobalt, lanthanum, manganese, nickel), and the synthetic antagonist verapamil on cerebral cortical neurons was examined. The results suggest that the depressant action of the calcium antagonists results either from their having a calcium like action on the membrane, or more likely from their displacement of calcium from binding sites on the membrane. The displaced calcium then acts in a manner analogous to topically applied calcium, depressing cell excitability. Subsequent applications of the calcium antagonists fail to depress cell excitability as a result either of a blockage of the calcium channels or of the absence of displaceable calcium. At this point, the biogenic amines also fail to depress neuronal excitability. 38 references. (Author abstract modified)

187807 Gauthier, Pierre; Nadeau, Reginald A.; de Champlain, Jacques. Department of Physiology, School of Medicine, University of Montreal, Montreal, Quebec H3C 3T8 **Cardiovascular reactivity in the dog after chemical sympathectomy with 6-hydroxydopamine.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):590-601, 1974.

The cardiovascular responses to intravenous injections of noradrenaline, isoproterenol, and phenylephrine were studied in unanesthetized and anesthetized dogs before and after chemical sympathectomy with 6-hydroxydopamine (6-OH-DA). Three days after 6-OH-DA pretreatment, the blood pressure response to noradrenaline in unanesthetized dogs was increased significantly despite the presence of a marked reflex slowing of the heart. Chronotropic and pressor responses to noradrenaline were likewise increased in anesthetized and vagotomized dogs after 6-OH-DA pretreatment. Not only was the amplitude of the responses to noradrenaline increased after 6-OH-DA pretreatment but their duration was likewise prolonged. In contrast, the cardiovascular responses to isoproterenol and phenylephrine did not appear significantly changed in 6-OH-DA pretreated dogs. These results are consistent with the development of a presynaptic type of supersensitivity in dogs pretreated with 6-OH-DA. 22 references. (Author abstract modified)

187831 Fuller, Ray W.; Perry, Kenneth W. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Methiothepin elevation of 5-hydroxyindoleacetic acid levels in various anatomic regions of rat brain.** Brain Research (Amsterdam). 70(2):369-371, 1974.

The effect of methiothepin on 5-hydroxyindole levels was investigated in various regions of the rat brain. Methiothepin significantly elevated 5-hydroxyindoleacetic acid (5HIAA) levels but not central serotonin (5HT) levels in whole brain of rats. Levels of 5HIAA were increased most in the cerebral hemispheres, medulla, and hypothalamus, with the least significant change being in the midbrain. Levels in the cerebellum were very low and were not affected by methiothepin. Levels of 5HT were not changed by methiothepin in any brain region. The increases in 5HIAA levels presumably result from increased 5HT turnover secondary to blockade of central 5HT receptors by methiothepin. 6 references.

187835 Cottee, Lynne J.; Van der Steen, Jennifer A.; Burke, W. University of Sydney, N.S.W. 2006, Australia **PGO waves in the lateral geniculate nucleus triggered by barbiturate.** Brain Research (Amsterdam). 70(2):205-219, 1974.

Slow phasic potential changes in the lateral geniculate nucleus (LGN) of the cat under pentobarbitone anesthesia are described. A detailed comparison was made between these waves and the ponto - geniculo - occipital (PGO) waves of low voltage fast sleep. It was concluded that the waves occurring during barbiturate anesthesia are essentially the same as the PGO waves and that they result from a triggering of the same mechanism. PGO-barbiturate (GO-B) waves and PGO waves recorded from the same site in the LGN are both negative waves and both reverse to positive waves below the LGN; both are discrete and show only limited amplitude and waveform variation; both appear in episodes; both occur synchronously in the two LGNs, in the visual cortex and in the pontine reticular formation but they are not present in the optic tract. Differences between the two types of wave are mainly quantitative. 35 references. (Author abstract modified)

187923 Gillis, Richard A.; Pearle, David L.; Hoekman, Theodore. Dept. of Pharmacology, Georgetown University, Schools of Medicine and Dentistry, Washington, DC 20007 **Failure of beta-adrenergic receptor blockade to prevent arrhythmias induced by sympathetic nerve stimulation.** Science. 185(4145):70-72, 1974.

Failure of beta-adrenergic receptor blockade to prevent arrhythmias induced by ventrolateral cardiac sympathetic nerve (VLCN) stimulation was studied, exploring whether previously applied beta-receptor blocking agents were insufficient or if these synapses differ from the usual sympathetic neuroeffector junctions in a more fundamental way. Cardiac arrhythmias

produced by electrical stimulation of the ventrolateral cardiac sympathetic nerve in dogs were not blocked by the combined administration of propranolol and practolol in amounts that completely blocked cardiac beta-adrenergic receptors. Blockade of cardiac alpha-adrenergic receptors, as well as cardiac cholinergic receptors, also had no influence on the arrhythmias. These results suggest that the adrenergic neuroeffector junction is fundamentally different from any hitherto described, differing perhaps in the neurotransmitter involved or in the nature of the receptor. 17 references. (Author abstract modified)

187928 Abel, E. L.; McMillan, D. E.; Harris, Louis S. New York State Department of Mental Hygiene, Research Institute on Alcoholism, Buffalo, NY 14203 **Delta9-tetrahydrocannabinol: effects of route of administration on onset and duration of activity and tolerance development.** Psychopharmacologia (Berlin). 35(1):29-38, 1974.

Pigeons trained to key peck for food reinforcement on a VI 3' were injected either orally, intramuscularly, or intravenously with delta9-tetrahydrocannabinol and the onset and duration of the drug were determined. Onset of action was much faster for the intravenous route than the other two routes. Speed and duration of effect were also affected by drug dosage. Using the same methods, the development of tolerance to the behavioral effects were investigated. Tolerance occurred with all three routes at about the same rate. 22 references. (Author abstract)

187931 David, Joy; Grewal, R. S.; Wagle, G. P. CIBA Research Centre, Post Bag 9002, Aarey, Rd., Goregaon, Bombay 400063, India **Persistent electroencephalographic changes in rhesus monkeys after single doses of pentobarbital, nitrazepam and imipramine.** Psychopharmacologia (Berlin). 35(1):61-75, 1974.

The immediate and persistent effects of single oral doses of sodium pentobarbital 20mg/kg, nitrazepam 24mg/kg, and imipramine 25mg/kg, were compared on behavioral patterns as well as on quantitative aspects of diurnal electroencephalographic (EEG) patterns in rhesus monkeys. Consecutive predrug EEG recordings on agar treated monkeys showed no significant variations in day to day EEG levels of wakefulness, drowsiness, sleep and the rapid eye movement (REM) state. Both sedative hypnotic agents significantly reduced wakefulness and the REM state and increased slow wave sleep. The antidepressant agent imipramine did not influence any of the EEG parameters. Significantly enhanced REM levels persisted during the 7 day postdrug period after cessation of medication of all three psychoactive agents. 17 references. (Author abstract modified)

187935 Nadler, R. D. Yerkes Regional Primate Research Center, Emory University, Atlanta, GA 30322 **Further evidence on the intrahypothalamic locus for androgenization of female rats.** Neuroendocrinology. 12:110-119, 1973.

Experiments are reported which were conducted in order to gain further evidence on the locus for inducing the anovulatory syndrome by implanting micropellets of androgen that were smaller than those used in previous studies, and by implanting pellets whose size was related to the size of the hypothalamic nuclei to which they were directed. Female rats, 5 days of age, received micropellets of a testosterone - propionate (TP - paraffin mixture in the brain or under the skin, pellets of paraffin alone in the brain, or no treatment. The only animals that developed the acyclic, anovulatory syndrome as adults were those that had TP implanted in the brain. The most effective site for producing the syndrome was the ventromedial - arcuate area of the hypothalamus. The shortest latencies to onset of the syndrome occurred in animals with TP at the anterior portion of the arcuate nucleus. (Author abstract)

188164 Hamon, Michel; Bourgoin, Sylvie; Jagger, Janine; Glowinski, Jacques. Laboratoire de Biologie Moleculaire, College de France, Paris 5e **Effects of LSD on synthesis and release of 5-HT in rat brain slices.** Brain Research (Amsterdam). 69(2):265-280, 1974.

The effects of LSD on 5-hydroxytryptamine (5-HT) metabolism were studied in rat hippocampal and striatal slices. One hour after in vivo treatment with the drug, and the synthesis of (3H)5-HT from L-(3H)tryptophan ((3H)Try) was only decreased in the striatum. This effect was associated with a significant reduction in the accumulation of (3H)Try in tissues, whereas endogenous levels of Try in the striatum and hippocampus were significantly increased by this treatment. Such modifications of 5-HT metabolism could not be reproduced by adding LSD directly into the incubating medium of control slices. The release of (3H)5-HT, synthesized from (3H)Try or taken up by tissues, was very much increased when concentrations of K+ in the incubating medium reached 30 or 50mM. This effect was countered by LSD, administered previously in vivo or added in vitro. High concentrations of LSD added in vivo induced a reserpine like effect on newly synthesized as well as exogenous (3H)5-HT. 35 references. (Author abstract modified)

188167 Askew, William E.; Kimball, A. P.; Ho, Beng T. Texas Research Institute of Mental Sciences, Houston, TX 77025 **Effect of tetrahydrocannabinols on brain acetylcholine.** Brain Research (Amsterdam). 69(2):375-378, 1974.

Effects of delta9-tetrahydrocannabinol (THC), delta8-THC and its major metabolite, 11-hydroxy-delta8-THC (11-HO-delta8-THC) on brain acetylcholine (ACh) were studied in the rat. Delta8-THC and delta9-THC produced a marked depletion of ACh in the rat brain, while 11-HO-Delta8-THC had no significant effect on ACh content. No significant decrease in choline acetyltransferase activity was found in the brain of delta8-THC treated animals. Results suggest that delta8-THC exerts its anticholinergic effect by increasing the release of ACh which, upon subsequent degradation, decreases its amount for neurotransmission. 11 references.

188178 Masten, Lawrence W.; Peterson, George R.; Burkhalter, Alan; Way, E. Leong. Dept. of Pharmacology, University of California Medical Center, San Francisco, CA 94143 **Effect of oral administration of methadone on hepatic microsomal mixed function oxidase activity in mice.** Life Sciences (Oxford). 14(9):1635-1640, 1974.

The effect of oral administration of methadone on hepatic drug metabolizing enzymes was studied in mice. Daily administration brought about a twofold increase in the activity of liver N-demethylase within a few days and maintained this high level of activity for the 30 day duration of the experiment. An increase in hepatic microsomal protein and a decrease in pentobarbital sleeping times were noted in the methadone treated animals. Subcutaneous administration of methadone for 6 days resulted in a much smaller increase in the activity of N-demethylase. 10 references. (Author abstract modified)

188196 Jori, Armanda; Cecchetti, Giancarlo; Ghezzi, Daniela; Samanin, Rosario. Istituto di Ricerche Farmacologiche Mario Negri, via Eritrea, 62, 20157 Milano, Italy **Biochemical and**

behavioral antagonism between fenfluramine and apomorphine in rats. European Journal of Pharmacology (Amsterdam). 26(2):179-183, 1974.

Biochemical and behavioral antagonism between fenfluramine and apomorphine was studied in rats. Pretreatment with apomorphine markedly antagonized the increase of homovanillic acid induced by fenfluramine. In contrast, the effect of amphetamine on homovanillic acid was not affected by apomorphine pretreatment. Fenfluramine significantly reduced the apomorphine stereotype in a dose dependent manner. It is suggested that fenfluramine acts on striatal dopamine by a mechanism similar to that of neuroleptics. 38 references. (Author abstract modified)

188198 DeQuattro, Vincent; Alexander, Natalie. White Memorial Medical Center, Los Angeles, CA 90033 **Altered norepinephrine synthesis of splanchnic vessels in neurogenic hypertension.** European Journal of Pharmacology (Amsterdam). 26(2):231-235, 1974.

Neurotransmitter metabolism and vascular resistance in splanchnic vessels of sino aortic denervated (SAD) rabbits were examined. SAD was found to produce neurogenic hypertension which was characterized first by increased cardiac output and later by increased peripheral vascular resistance. Tyrosine hydroxylase activity and catecholamine concentration of proximal mesenteric artery were greater than those of distal mesenteric vessels in normal rabbits. One hour after SAD, norepinephrine (NE) synthesis, the activity of tyrosine hydroxylase assayed in vitro, was increased in proximal mesenteric artery and decreased in distal mesenteric vessels. Eleven and 30 days after SAD, NE synthesis in vivo and the activity of tyrosine hydroxylase assayed in vitro was increased in distal mesenteric vessels and decreased in mesenteric artery. Sympathoadrenal regulation of increased splanchnic vascular resistance may be an important factor in the initiation and maintenance of neurogenic hypertension in the rabbit. 20 references. (Author abstract modified)

188199 Tsujimoto, A.; Nishikawa, T.; Dohi, T.; Kojima, S. Dept. of Pharmacology, Hiroshima University School of Dentistry, Hiroshima, Japan **Comparison of pharmacological responses to nicotine and release of catecholamines from the adrenals in dogs and monkeys.** European Journal of Pharmacology (Amsterdam). 26(2):236-242, 1974.

Comparative studies were made on the metabolic and physiological responses to nicotine and epinephrine and on the release of catecholamines from the adrenal glands of dogs and monkeys by nicotine. Dogs were approximately 10 times more sensitive to nicotine than monkeys to responses such as hyperglycemia, hyperlipidaemia, increase in respiratory rate, heartrate and pressor responses. However, the metabolic, pressor and tachycardiac responses of the two species to epinephrine were very similar quantitatively. The plasma concentrations of catecholamine in the vena cava of dogs and monkeys were significantly increased by intravenous doses of 50 and 400 micrograms/kg of nicotine, respectively. The differences in the pharmacological responses to nicotine of dogs and monkeys, except that of respiration, may result in part from the less potent effect of nicotine in catecholamine release in monkeys than in dogs. 40 references. (Author abstract)

188200 Muller, E. E.; Cocchi, D.; Jalanbo, H.; Udeschini, G.; Peruzzi, G.; Mantegazza, P. Dept. of Pharmacology, University of Milan, Milan, Italy **Central hypothermia by 2-deoxy-D-glucose: antagonism by alpha-adrenergic activation.** European Journal of Pharmacology (Amsterdam). 26(2):243-255, 1974.

Various drugs were administered to rats to investigate whether 2-deoxy-D-glucose (2-DG) induced hypothermia might be altered by the functional activation or suppression of brain neurotransmitter substances. Hypothermia was induced by injection of 2-DG, a glucose analog, into the lateral brain ventricle and was followed by systematic administration of amphetamine, pimozide, clonidine, FLA-63 and alpha-methyl-p-tyrosine. Results suggest that the body temperature fall due to central glucopenia is antagonized by the activation of a central norepinephrine (NE) mechanism, and conversely potentiated by reduction of central NE tone. During the hypothermia induced by glucoprivation, central catecholamines, namely NE, would provide a link for the physiological activation of heat gain mechanisms through the adrenal medulla and sympathetic nervous system. 52 references. (Author abstract modified)

188201 Lodge, David; Headley, P. Max; Duggan, Arthur W.; Biscoe, Tim J. Dept. of Physiology, Medical School, University Walk, Bristol, BS8 1TD, England **The effects of morphine, etorphine and sinomenine on the chemical sensitivity and synaptic responses of Renshaw cells and other spinal neurones in the rat.** European Journal of Pharmacology (Amsterdam). 26(2):277-284, 1974.

The effects of electrophoretically applied morphine, etorphine and sinomenine were investigated on Renshaw cells and other spinal neurons of the rat, and only morphine specifically reduced the depressant effect of glycine without affecting that of gamma aminobutyric acid. On Renshaw cells, only morphine increased the response to acetylcholine more than that to D,L-homocysteate, and increased the latency of the action potentials which follow a ventral root stimulus. The differences between the effects of morphine and those of etorphine and simonenine suggest that those properties of the drugs investigated in this study are not related to the analgesic properties of morphine and etorphine. 26 references. (Author abstract modified)

188202 Pruitt, David B.; Grubb, Margaret N.; Jaquette, Dale L.; Burks, Thomas F. Dept. of Pharmacology, University of Texas Medical School, Houston, TX 77025 **Intestinal effects of 5-hydroxytryptamine and morphine in guinea pigs, dogs, cats and monkeys.** European Journal of Pharmacology (Amsterdam). 26(2):298-305, 1974.

To establish the intestinal effects of morphine and 5-hydroxytryptamine (5-HT) by similar techniques in different species, intestinal introluminal pressure was measured in vivo in guinea pigs, dogs, cats, and monkeys. In guinea pigs, but not in the other species, the intestinal stimulatory effect of 5-HT was antagonized by morphine. The 5-HT blocking action of morphine in intestine seems to be unique to the guinea pig. 24 references. (Author abstract modified)

188204 Cheng, Hsien C.; Long, John P. Dept. of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Dopaminergic nature of apomorphine-induced pecking in pigeons.** European Journal of Pharmacology (Amsterdam). 26(2):313-320, 1974.

The mechanism by which apomorphine induces pecking in pigeons was studied, and the effects of various drugs on this pecking response were examined. The pecking induced by apomorphine (1.64 micromole/kg) has a rapid onset and lasts for approximately one hour. The response can be blocked by dopaminergic receptor blocking agents such as chlorpromazine, haloperidol, bulbocapnine and morphine but not by alpha-adrenergic or beta-adrenergic receptor blocking agents.

Cholinergic agents have an inhibitory effect on pecking. The inhibitory effect of oxotremorine can be reversed by prior administration of atropine. Apomorphine can induce both pecking and emesis while apomorphine methiodide causes only emesis. Findings indicate that the pecking induced by apomorphine is caused by the stimulation of central dopaminergic receptors and that central chlorinergic systems have a modulating effect on pecking. Serotonergic systems might also inhibit the pecking induced by apomorphine. 33 references. (Author abstract modified)

188231 Yagiela, John A.; McCarthy, Ken D.; Gibb, James W. Dept. of Biopharmaceutical Sciences, College of Pharmacy, Univ. of Utah, Salt Lake City, UT 84112 **The effect of hypothermic doses of 1-delta9-tetrahydrocannabinol on biogenic amine metabolism in selected parts of the rat brain.** Life Sciences (Oxford). 14(12):2367-2378, 1974.

Hypothalamic and brainstem biogenic amine metabolism was investigated in rats following the administration of hypothermic doses of 1-delta9-tetrahydrocannabinol (THC). The dose dependent fall in body temperature induced by THC was both rapid in onset and prolonged in duration. The disruption in thermoregulation, however, was unaccompanied by any observed alteration in the concentration or turnover rate of 5-hydroxytryptamine (5-HT) in the brain tissues studied. Norepinephrine (NE) was also unchanged, with the exception of a reduction in the amount of brainstem NE 30 min after the administration of 50mg/kg THC. These observations indicate that the hypothermic effect of THC is not mediated by changes in brain 5-HT or NE metabolism. 26 references. (Author abstract modified)

188287 Victor, S. J.; Baumgarten, H. G.; Lovenberg, W. Section on Biochemical Pharmacology, Experimental Therapeutics Branch, National Heart and Lung Institute, NIH, Bethesda, MD 20014 **Depletion of tryptophan hydroxylase by 5,6-dihydroxytryptamine in rat brain -- time course and regional differences.** Journal of Neurochemistry (Oxford). 22(4):541-546, 1974.

Wistar rats were injected intraventricularly with 75 micrograms 5,6-dihydroxytryptamine in order to study the depletion of tryptophan hydroxylase. Tryptophan hydroxylase was assayed in seven regions of the brain, as well as the spinal cord, at intervals following injection. The spinal cord was depleted to 1% of control by 12 days; tectum was depleted to 32% of control by 9 days. The time course of depletion in most regions was biphasic, with an early reduction of activity 1 h after injection, with continued reduction of activity 1-2 days following injection, and a recovery of activity at 4-6 days. The activity again drops at 9-12 days, and this reduction of activity persists to varying degrees to 60 days, with slight recovery at this time in certain regions. 25 references. (Author abstract)

188291 Edwards, C.; Nahorski, S. R.; Rogers, K. J. Section of Pharmacology, Academic Division of Medicine, University of Sheffield, Sheffield S10 2TN, England **In vivo changes of cerebral cyclic adenosine 3',5'-monophosphate induced by biogenic amines: association with phosphorylase activation.** Journal of Neurochemistry (Oxford). 22(4):565-572, 1974.

Evidence is presented that adenosine 3',5'-monophosphate (cyclic AMP) may be involved in the activation of cerebral phosphorylase and the subsequent glycogenolysis induced by certain biogenic amines. The intravenous injection of adrenaline, isoprenaline and histamine to 4-6-day-old chicks resulted in a rapid increase in the cyclic AMP content of cerebral hemispheres that had been removed and frozen. Noradrenaline, dopamine, adenosine, 5-HT and acetylcholine did not significantly alter the nucleotide concentration in vivo. Addition of adrenaline, isoprenaline and histamine to incubated chick cerebral cortex slices also increased the cyclic AMP content of the tissue. Noradrenaline was considerably less potent and adenosine was ineffective. It is suggested that in vivo phosphorylase activation and subsequent glycogenolysis may occur, at least in part, in glia and that these cells may be damaged during preparation of cerebral slices. The results provide evidence of a metabolic role for cyclic AMP in cerebral tissue. 47 references. (Author abstract modified)

188374 Gloor, P.; Testa, G. Montreal Neurological Institute, 3801 University Street, Montreal, Quebec **Generalized penicillin epilepsy in the cat: effects of intracarotid and intravertebral pentylenetetrazol and amobarbital injections.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 36(5):499-515, 1974.

The similarities between a feline form of epilepsy caused by injections of pentylenetetrazol and amobarbital and human generalized corticoreticular epilepsy are illustrated. The origin of the convulsive discharges in the animal model is thought to be cortical. Brain stem structures, however, exert a powerful influence upon these discharges: increased desynchronizing drive of brain stem reticular origin markedly reduces or even eliminates them; conversely a reduction in ascending reticular drive markedly promotes their occurrence. It is proposed that similar mechanisms are at work in human generalized corticoreticular epilepsy. 36 references. (Author abstract modified)

188393 de Wied, David; de Jong, Wybren. Rudolf Mangus Institute for Pharmacology, University of Utrecht, Utrecht, The Netherlands **Drug effects and hypothalamic-anterior pituitary function.** In: Elliott, H., Annual review of pharmacology. Palo Alto, CA, Annual Reviews, 1974. 594 p. (p. 389-412). v. 14.

A discussion is given of recent data concerning the neuroendocrine control of anterior pituitary function, which has been studied with the use of drugs that affect the release of hypothalamic hypophysiotropic factors through their action of brain neurotransmitters. The evidence supports the hypothesis that monoamines and other transmitter substances participate in the control of hypophysiotropic hormones from the releasing factor cells in the median eminence of the hypothalamus. These cells can be regarded as neuroendocrine transducer cells that differ from neurons as well as from endocrine cells in that they convert a neuronal input to a humoral output. 206 references.

188404 Hadfield, M. Gary; Bosworth, James E. Department of Pathology, Medical College of Virginia, Division of Neuropathology, Virginia Commonwealth University, Richmond, VA 23298 **In vitro binding of (4-14C) diphenylhydantoin to rat brain microsomes.** Brain Research (Amsterdam). 71(1):183-186, 1974.

In vitro binding of (4-14C)diphenylhydantoin (DPH) to rat brain microsomes was investigated. Microsomes, obtained from both animals that had received chronic high doses of DPH and those that had received saline, bound less than .34% of the (4-14C)DPH to which they were exposed, and there was no significant difference in binding between the two groups. Though many in vivo studies have shown that DPH has an affinity for the microsomal fraction, the in vitro binding of DPH to microsomes in the present experiments was only 2-3% of that reported in in vivo studies. The present in vitro data indicate that microsomes, in and of themselves, have little abili-

ty to bind with DPH. DPH may enter microsomes (endoplasmic reticulum) indirectly, presumably via the nucleus. 13 references.

188406 Jus, K.; Jus, A.; Gautier, J.; Villeneuve, A.; Pires, P.; Pineau, R.; Villeneuve, R. Research Department, Hospital St.-Michel-Archange, Quebec 05, P.Q., Canada **Studies on the action of certain pharmacological agents on tardive dyskinesia and on the rabbit syndrome.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(2):138-145, 1974.

Results are given on clinical and polygraphic studies on the influence on tardive dyskinesia and on the rabbit syndrome of intravenously administered single doses of benztropine mesylate, diazepam, diphenylhydantoin, and orally administered single doses of D-L tryptophan. Benztropine mesylate was effective in the rabbit syndrome, whereas in tardive dyskinesia it provoked only a short time decrease of the muscle tone. Diazepam was effective in both conditions, but provoked a simultaneous decrease in the level of vigilance. Diphenylhydantoin was effective in about 50% of tardive dyskinesia and ineffective in the rabbit syndrome. D-L tryptophan was ineffective in both conditions, and a significant difference was found in the values of excretion of kynurenine pathway metabolites after D-L tryptophan loading between the patient group and the control group. The possible mechanisms of actions of all these drugs are discussed, and on the basis of the findings the study of long-term diphenylhydantoin administration is proposed. 36 references. (Journal abstract modified)

188424 Fowler, Glenn W.; Julien, Robert M. Irvine, CA **Imipramine in experimental petit mal epilepsy.** Neurology. 24(4):369, 1974.

The effectiveness of imipramine was evaluated in cats using estrogen induced seizures resembling petit mal epilepsy in humans. Pentylene - tetrazol seizures do not resemble the petit mal attacks nor estrogen induced seizures in animals electroencephalographically and behaviorally. It was found that imipramine was effective in blocking the 3 Hz spike - wave EEG discharges induced by estrogen. No further improvement was found in dosages about 5mg/kg, and some animals developed a polyspike EEG pattern and major seizures at that dosage. A double dose of imi pramine consistently produced a change in the EEG to diffuse polyspikes that was usually associated with major seizures. The results of this study are seen as supporting previous work on the usefulness of imipramine for epileptic treatment. However, it appears that the antiepileptic effect of this drug occurs at relatively low doses. Caution should be used in giving any larger amounts of imipramine to children. (Journal abstract modified)

188426 Stahl, Stephen M.; Daniels, A. C.; Derda, D.; Spehlmann, R. Chicago, IL **Intracerebral injection of 6-hydroxydopamine and hydrogen peroxide in cats: specific and nonspecific effects on striatal biogenic amines.** Neurology. 24(4):371-372, 1974.

The reduction of catecholamines in caudate nucleus by the injection of intracerebral 6-hydroxydopamine (6OHDA) was studied in cats. Catecholaminergic neurons will either be destroyed directly by 6OHDA or hydrogen peroxide will be liberated to destroy them. Nigral injection of high doses of either agent or low doses of 60HDA decreased catecholamine and induced similarly nonselective histologic damage in the substantia nigra. Serotonin and catecholamines were reduced by high doses of 60HDA and H2O2. The catecholamine depleting effects of low doses of nigral 60HDA injections were significantly potentiated by inhibiting brain monoamine oxidase by 90% or more. The results suggest that the liberation of H2O2 from 6OHDA could explain some possible nonspecific effects of high doses of 6OHDA; at lower doses, however, 6OHDA may have specific effects on catecholamine not mediated by hydrogen peroxide. (Journal abstract modified)

188433 Wasterlain, Claude G.; Sweet, Richard D. New York, NY **Disaggregation of brain polysomes after L-dopa: an analysis.** Neurology. 24(4):398, 1974.

Changes in brain polyribosomes following administration of L-dopa in rats are reported. It was discovered that L-dopa induced ribosomal monomers and dimers were completely and reversibly dissociated into ribosomal subunits in high ionic strength buffers unless prefixed in formaldehyde. Brain ribosomes from L-dopa treated rats incorporated less radioactive leucine into proteins than control ribosomes, but were as readily stimulated by another injection. These properties suggest a block of initiation of protein synthesis in the brain of dopa treated rats, and a possible link between changes in brain transmitter levels and changes in brain protein synthesis. These findings may be relevant to some of the complications of L-dopa therapy. (Journal abstract modified)

188519 Tagliamonte, A.; Fratta, W.; Gessa, G. L. Institute of Pharmacology, Univ. of Cagliari, Via Porcell 4, I-09100 Gagliari, Italy **Aphrodisiac effect of L-DOPA and apomorphine in male sexually sluggish rats.** Experientia (Basel). 30(4):381-382, 1974.

The aphrodisiac effect of L-DOPA and apomorphine was examined in male sexually sluggish rats. Results showed that either apomorphine or a combination of Ro 4-4602 with L-DOPA increased the copulatory behavior of sexually sluggish male rats and that this effect was prevented by haloperidol. In addition, haloperidol suppressed the spontaneous copulatory behavior of rats with high level of sexual activity. Results suggested that brain dopamine stimulates copulatory behavior in male rats. 9 references.

188739 Stone, Trevor W. Department of Physiology, University of Aberdeen, Marischal College, Aberdeen, Scotland **Further evidence for a dopamine receptor stimulating action of an ergot alkaloid.** Brain Research (Amsterdam). 72(1):177-180, 1974.

The effects of agroclavine applied directly to central neurons were examined in the rat. The results of applying agroclavine and dopamine and either noradrenaline or 5-hydroxytryptamine (5-HT) to 45 active units revealed that 78% of the cells tested responded in the same way to agroclavine and dopamine whereas only 48% responded in the same manner manner to agroclavine and noradrenaline of 5-HT. The data suggests that agroclavine could be acting on dopamine receptors. The application of chorpromazine blocked the response to dopamine and agroclavine and left 5-HT responses unaffected. It is concluded that agroclavine and other ergot alkaloids may have an agonistic action at central dopamine receptors. 15 references.

188750 Bennett, J. L.; Aghajanian, G. K. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **The effect of p-chlorophenylalanine on forebrain tryptophan hydroxylase in rats with lesions in the raphe nucleus.** Brain Research (Amsterdam). 65(3):537-541, 1974.

The effect of p-chlorophenylalanine (PCPA) on forebrain tryptophan hydroxylase (TH) was examined in rats with lesions in the raphe nucleus. The administration of PCPA to

nonlesioned rats resulted in a gradual inactivation of the enzyme in all four forebrain regions. TH activity in raphe lesioned rats not given PCPA fell slowly over the first 3 days in all regions of the forebrain; on the third day the levels in the various regions were about 50% below the nonlesioned rats. TH activity in the various forebrain regions of the raphe lesioned rats, given PCPA immediately after the placement of the lesion, fell in a manner which was virtually identical to the drug treated nonlesioned rats. Results indicate that the irreversible inactivation of TH by PCPA can still take place in the absence of that site (raphe nuclei) which is presumably responsible for the synthesis of the enzyme. 20 references. (Author abstract modified)

188751 Proudfit, Herbert K.; Anderson, Edmund G. Department of Pharmacology, University of Illinois, College of Medicine, Chicago, IL 60680 **New long latency bulbospinal evoked potentials blocked by serotonin antagonists.** Brain Research (Amsterdam). 65(3):542-546, 1974.

New long latency bulbospinal evoked potentials blocked by serotonin antagonists in the cat brain are reported. In decerebellate cats stimulation of areas in the caudal brainstem having 5-hydroxytrptamine (5-HT) containing cell bodies evoked complex potentials in both the dorsal and ventral roots of the lumbar cord. The long latency of the dorsal root potentials-2 and ventral root potentials-2 was consistent with the slow conduction velocity expected from the small diameter serotonergic axons which descend from the caudal raphe. The blockade of the long latency potentials by the administration of two chemically different 5-HT antagonists, cinanserin and methysergide, provides evidence that these potentials are mediated by 5-HT. A descending serotonergic system composed of two basic divisions is postulated: 1) affecting motoneurons; and 2) contacting interneurons along pathways which ultimately terminate presynaptically on Group I primary afferent terminals. 13 references.

188769 Symes, Aston L.; Sourkes, Theodore L. Department of Biochemistry, Queen Mary Veterans' Hospital, Montreal 247, Quebec, Canada **Pharmacological and biochemical actions of the hemolytic agents acetylphenylhydrazine and phenylhydrazine on monoamine oxidase in the rat.** Biochemical Pharmacology (Oxford). 23(14):2045-2056, 1974.

Pharmacological and biochemical actions of the hemolytic agents acetylphenylhydrazine (APHZ) and phenylhydrazine (PHZ) on monoamine oxidase (MAO) were studied in the rat. The injection of normal rats with APHZ and PHZ rapidly produces a long lasting inhibition of MAO. The effect is more pronounced in liver than in brain. APHZ inhibits liver MAO more actively than does an equivalent dose of PHZ. The former compound causes 65-75 per cent inhibition of activity by 24 hr after injection, whereas PHZ inhibits by about 40 per cent at 24 hr and 50 per cent at 2 days. On the other hand, PHZ is slightly more active than APHZ against the rat brain enzyme in vivo. The inhibitory effects of APHZ in vivo are enhanced in riboflavin-deficient rats. Both drugs inhibit MAO in vitro in an immediate, irreversible, noncompetitive manner; inhibition is independent of pH. PHZ is more active than APHZ against rat liver MAO. 58 references. (Author abstract modified)

188864 Lechat, P.; Auclair, M. C.; Adolphe, M. Institut de Pharmacologie, U.E.R. Biomedicale des Cordeliers, Paris, France **Effect of imipramine on cultured rat heart cells.** Toxicology and Applied Pharmacology. 27(2):336-341, 1974.

The effect of imipramine on cultured rat heart cells is reported. Imipramine, after 5 min of contact stopped the beating of cultured rat myocardial cells. The inhibition of beating was suppressed in a potassium (K) free medium. Imipramine after 3 days of contact induced a vacuolization of both musclelike and fibroblastlike cells in a medium with or without K. This effect appeared to be nonspecific for cardiac cells since it was also induced by imipramine on HeLa cells. The possibility exists that imipramine may act on the cultured heart cells by two different mechanisms: 1) could be related to an effect on membrane permeability; 2) occurring later, could result from a general cytotoxic effect. 23 references. (Author abstract modified)

188873 Sohel, M. S.; Brahamankar, D.M.; Chopde, C. T.; Dorle, A. K. Department of Pharmaceutical Sciences, Nagpur University, Nagpur, India **Influence of adrenergic blockers and antilipemic agents on pharmacodynamic actions of morphine in carbon tetrachloride-treated rats.** Toxicology and Applied Pharmacology. 27(3):477-483, 1974.

Influence of adrenergic blockers and antilipemic agents on pharmacodynamic action of morphine in carbon tetrachloride (CCl_4) treated rats was studied. The analgesic activity of morphine was markedly prolonged in rats by 24 hr pretreatment with carbon tetrachloride. The urinary excretion of morphine was drastically reduced in these rats indicating impairment in morphine metabolism. However, pretreatment with alpha and beta adrenergic blockers or 20 hr posttreatment with antilipemic agents greatly diminished the CCl_4 induced prolongation of analgesic activity. These agents also increased the urinary morphine excretion that was reduced by CCl_4 treatment. All the adrenergic blockers except propranolol and both antilipemic agents caused a significant reduction in the lipid content of the liver. Since the liver fat plays a significant role in hemodynamic resistance induced by CCl_4 treatment, the protection afforded by adrenergic blockers and antilipemic agents to the drug metabolizing enzyme system could be related to their lipid lowering activity. 38 references. (Author abstract)

188891 Trabucchi, M.; Cheney, D.; Racagni, G.; Costa, E. Lab. of Preclinical Pharmacology, St. Elizabeth's Hospital, Washington, D C 20032 **Involvement of brain cholinergic mechanisms in the action of chlorpromazine.** Nature(London). 249(5458):664-666, 1974.

An investigation of whether the action of chlorpromazine or haloperidol is associated with a change in the activity of brain cholinergic neurons is reported. The effect of chlorpromazine and haloperidol on the turnover rate of acetylcholine (ACh) in the occipital cortex and striatum of rats was monitored to assess whether the synthesis of ACh in various areas of rat brain is increased when dopamine receptors are blocked. The amount of ACh synthesized in the striatum of rats receiving chlorpromazine or haloperidol 1h before the infusion of phosphorylcholine was increased: there was no similar increase in the occipital cortex. These findings minimize the possibility that nonspecific effects of the two drugs are operative in explaining the increase of ACh turnover rate: actually they suggest that these two drugs affect some neuronal mechanism that is important in the control of striatal ACh synthesis and less important in the control of the synthesis of ACh in the occipital cortex. 19 references.

188914 Lorkovic, H. Neurosensory Center, University of Iowa College of Medicine, Iowa City, IA 52240 **Effect of divalent cations on ACh contractures of depolarized denervated rat muscles.** American Journal of Physiology. 226(6):1286-1292, 1974.

The effect of divalent cations on ACh contractures of depolarized chronically denervated rat muscles was studied by soaking the muscles in Tris-Cl solutions containing potassium. Sucrose solutions containing calcium and magnesium or nickel were applied and contracture was provoked by ACh. It was concluded that the antagonism between calcium and the other divalent cations might suggest the presence in the membrane of some carrier molecules which are capable of inward transport of calcium when ACh is applied. 29 references.

188915 Kroeger, E. A.; Marshall, J. M. Dept. of Physiology, Faculty of Medicine, Univ. of Manitoba, Winnipeg, Canada **Beta-adrenergic effects on rat myometrium: role of cyclic AMP.** American Journal of Physiology. 226(6):1298-1303, 1974.

The role of cyclic AMP in the inhibition of the rat myometrium by beta-adrenergic agents is investigated. The inhibition caused by isoproterenol and papaverine, both of which increase tissue cAMP content, was qualitatively different from that caused by D-600, an analogue of verapamil which does not alter cAMP. Exposure of muscles to a calcium free solution accentuates the increase of tissue cAMP content produced by isoproterenol, while 2mM LaCl3 inhibits this response. Results are consistent with the hypothesis that cAMP plays a role in beta-adrenergic inhibition of the myometrium. 24 references. (Author abstract)

188976 Morot-Gaudry, Y.; Hamon, M.; Bourgoin, S.; Ley, J. P.; Glowinski, J. Laboratoire de Physiologie Acoustique CNRZ-INRA, Domaine de Vilvert, 78 Jouy-en-Josas, France **Estimation of the rate of 5-HT synthesis in the mouse brain by various methods.** Archives of Pharmacology (Berlin). 282(3):223-238, 1974.

Nonisotopic and isotopic methods used to estimate the rate of 5-HT synthesis in the mouse brain are discussed. 5-HT and 5-HIAA levels were measured in tissues up to 10 minutes after the injection of pargyline or pheniprazine. 5-HIAA levels were also estimated at various times after probenecid administration. 5-HTP levels were estimated at various times after the blockade of 5-HTP decarboxylase by Ro4-4602. Finally, the rate of conversion of tryptophan into 5-HT was estimated by measuring the initial accumulation of 3H-5-HT and 3H-5-HIAA in tissues following the intravenous injection of 3H-tryptophan. Rates of 5-HT synthesis obtained with the MAO inhibitor methods were higher. An intermediate rate of 5-HT synthesis was found with the isotopic technique. The high rate of 5-HT synthesis observed with the 5-HT, MAO inhibitor method was not related to a stimulation of 5-HT synthesis. Differences seen with all methods are discussed with respect to results obtained by various groups of workers. 43 references. (Author abstract modified)

188977 Baumgarten, H. G.; Groth, H. P.; Gothert, M.; Manian, A. A. Abteilung fur Neuroanatomie, Institut fur Pharmakologie, Universitat Hamburg, D-2000 Hamburg 20, Martinistr. 52, FRG **The effect of 5,7-dihydroxytryptamine on peripheral adrenergic nerves in the mouse.** Archives of Pharmacology (Berlin). 282(3):245-254, 1974.

Injections of 5,7-dihydroxytryptamine causing a significant reduction in the noradrenaline content of the mouse heart, large intestine, and seminal vesicle, 2 and 6 days after drug application, are discussed. The long lasting depletion of noradrenaline was found to be due to a degeneration of adrenergic nerve terminals as verified by fluorescence and electron microscopical observations. Results show that 5,7-dihydroxytryptamine is either as potent as or less potent than 6-hydroxydopamine in depleting noradrenaline. The pronounced effects of 5,7-dihyroxydopamine on the adrenergic nerves of the seminal vesicle suggest that 5,7-dihydroxytryptamine may be used as a tool for the induction of a chemical sympathectomy in certain peripheral organs of laboratory animals, supplementary to 6-hydroxydopamine. 21 references. (Author abstract)

188978 Tassin, J. P.; Thierry, A. M.; Blanc, G.; Glowinski, J. Groupe NB (INSERM U. 114) College de France, 11, Place Marcelin Berthelot, F-75 005 Paris 5e **Evidence for a specific uptake of dopamine by dopaminergic terminals of the rat cerebral cortex.** Archives of Pharmacology. 282(3):239-244, 1974.

To determine the existence of a specific dopamine uptake process in the cerebral cortex of the rat, the effects of desipramine and benztropine on 3H-dopamine uptake were investigated in homogenates obtained from tissues of sham operated rats and of rats injected locally with 6-OH-dopamine in order to destroy noradrenergic terminals. The results were compared with those obtained with striatal and cerebral homogenates. Desipramine inhibited completely 3H-dopamine uptake in the cerebellar cortex but only by 76% in the cerebral cortex of sham operated rates. Desipramine did not inhibit 3H-dopamine uptake in cerebral homogenates of rats pretreated with 6-OH-dopamine. However, the desipramine resistant 3H-amine uptake was reduced by benztropine. These results demonstrate the existence of a specific uptake of dopamine in the dopaminergic terminals of the rat cerebral cortex. 11 references. (Author abstract)

189026 Lidbrink, Peter; Jonsson, Gosta; Fuxe, Kjell. Department of Histology, Karolinska Institutet, S-104 01 Stockholm, Sweden **Selective reserpine-resistant accumulation of catecholamines in central dopamine neurones after DOPA administration.** Brain Research (Amsterdam). 67(3):439-456, 1974.

The capacity of central monoamine neurons to form and store catecholamines (CA), following administration of 3,4-dihydroxyphenylalanine (DOPA), was investigated in reserpine pretreated rats. Fluorescence histochemistry showed that selective accumulations of CA occur in previously known dopamine (DA) nerve terminals following treatment with DOPA together with a peripheral decarboxylase inhibitor of the subjects. These DA accumulations were depleted by amphetamine and associated with the appearance of marked stereotyped behavior. In vitro experiments with (3H)noradrenaline revealed that with a concentration of 10 micromoles but not with 0.1micromoles a selective accumulation of (3H)noradrenaline occurs in homogenates of neostriatum. The monoamine oxidase (MAO) activity in the neostriatum and the neocortex was not affected by reserpine pretreatment. It is suggested that the selective accumulation of CA in the DA nerve terminals in the presence of high amine concentrations results from reserpine resistant binding of CA to the DA granules. 44 references. (Author abstract modified)

189027 Costa, Marcello; Eranko, Olavi; Eranko, Liisa. Department of Zoology, University of Melbourne, Parkville 3052 Victoria, Australia **Hydrocortisone-induced increase in the histochemically demonstrable catecholamine content of sympathetic neurons of the newborn rat.** Brain Research (Amsterdam). 67(3):457-466, 1974.

Hydrocortisone induced increase in the histochemically demonstrable catecholamine content of sympathetic neurons of the newborn rat was studied. Subjects were subcutaneously injected with 20mg/kg bodyweight of hydrocortisone acetate each day for 5 days and were killed together with untreated controls 5 hours or 10 days after the last injection.

Histochemically demonstrable formaldehyde induced fluorescence was studied in the superior cervical ganglia, in the intestine, and in the iris. Hydrocortisone treatment caused a statistically significant increase in the number of intensely fluorescent nerve cell bodies and a corresponding decrease in the number of moderately fluorescent nerve cells in the superior cervical ganglia. In the Auerbach's plexus of subjects all fluorescent fibers were more clearly delineated than in controls. The network of adrenergic nerve fibers in the iris also significantly increased in fluorescence. It is concluded that hydrocortisone increases the content of noradrenaline in the sympathetic neurons. 21 references. (Author abstract modified)

189031 Cutler, Robert W. P.; Dudzinski, David S. Section of Neurology, Department of Medicine, University of Chicago, Chicago, IL 60637 **Effect of pentobarbital on uptake and release of (3H)GABA and (14C)glutamate by brain slices.** Brain Research (Amsterdam). 67(3):546-548, 1974.

The effect of pentobarbital on uptake and release of (3H)gamma-aminobutyric acid (GABA) and L-(14C)glutamic acid by slices of rat cerebral cortex was studied. Results indicate that pentobarbital inhibited significantly the slice uptake of L-(14C)glutamate. Similar results were obtained when the medium concentrations of the amino acids were lowered. The effect was greater at a high concentration of pentobarbital (5mM), a concentration which did not affect the uptake or release of (14C)urea. The rate of spontaneous efflux of (3H)GABA from the slices was also inhibited by pentobarbital, while the rate of spontaneous efflux of L-(14C)glutamate was scaracely affected. However, in the presence of 5mM pentobarbital, the rate of electrically induced release of (3H)GABA, but not of L-(14C)glutamate, was enhanced when a supramaximal electrical field stimulus was applied. Results show that pentobarbital preferentially affects the uptake and release of GABA. 6 references.

189032 David, R. J.; Wilson, W. A.; Escueta, A. V. Epilepsy Center, Veterans Administration Hospital, Durham, NC 27706 **Voltage clamp analysis of pentylenetetrazol effects on Aplysia neurons.** Brain Research (Amsterdam). 67(3):549-554, 1974.

Voltage clamp analysis of pentylenetetrazol (PTZ) effects on Aplysia neurons is reported. Previous studies have shown that PTZ induces bursting in normally silent Aplysia neurons, and current voltage characteristics change. Since PTZ induced bursting of normally autoactive cells, it was felt that a voltage clamp study might reveal previously undetected effects of the convulsant. The abdominal ganglion of Aplysia californica was removed from the animal and intracellular recordings were made via two KCl filled microelectrodes. Use of voltage clamping to construct I-V curves shows that silent cells which burst in the presence of PTZ display a region of negative slope resistance in their curves. Also, when bursting cells are silenced at 10 degrees C, PTZ restores bursting behavior. Results suggest that a voltage sensitive current source is responsible for the regenerative depolarization phase of PTZ induced oscillations and that negative resistance plays a role in PTZ induced seizures. 14 references.

189033 Barker, Jeffery L.; Levitan, Herbert. Behavioral Biology Branch, National Institute of Child Health and Human Development, NIH, Bethesda, MD 20014 **Phenols: effects on membrane permeability of molluscan neurons.** Brain Research (Amsterdam). 67(3):555-561, 1974.

The effects of phenols on membrane permeability of molluscan neurons were studied. Experiments were performed on large, identified neurons in the buccal ganglion of the marine mollusk Navanax inermis. The membrane potential and input resistance of neurons were monitored with intracellular electrodes. Cells were exposed to the sodium salt of a phenol dissolved in a saline solution just prior to perfusion. 2,4-Dinitrophenol (2,4-DNP) and other phenols tested reversibly increased the membrane potential and input conductance in a dose dependent manner. Activity is dependent on the nonspecific adsorbability of the phenol analog to the membrane, and not on any particular steric requirements. The phenol analogs increase membrane potential and conductance primarily by increasing the potassium conductance, and decreasing the chloride conductance. A change in relative cation permeability suggests that phenols increase potassium conductance and decrease chloride conductance by adsorbing to, and increasing the anionic field strength of neuronal membranes. 40 references.

189210 Messiha, F. S. Psychopharmacology Division, Department of Psychiatry, Texas Tech. University of Medicine, Lubbock, TX 79409 **A study of biogenic amine metabolites in the cerebrospinal fluid and urine of monkeys with chlorpromazine-induced dyskinesia.** Journal of the Neurological Sciences (Amsterdam). 21(1):39-46, 1974.

Biogenic amine metabolites in the cerebrospinal fluid and urine of monkeys with chlorpromazine induced dyskinesia were studied. Long-term administration of increasing doses of chlorpromazine (CPZ) in a daily dosage of 10-180mg produced dyskinetic involuntary movements in the buccolingual area of monkeys. The abnormal movements in the monkeys were associated with an increase in the concentration of dihydroxyphenylacetic acid, homovanillic acid and 5-hydroxyindoleacetic acid in the cerebrospinal fluid (CSF), as well as an increase in the urinary excretion of dopamine, 3-methoxytyramine and norepinephrine. Short-term administration of CPZ or haloperidol failed to alter either the neurological status or the level of catecholamine metabolites in the CSF and urine of the monkeys. The possible role of an increase in dopamine synthesis in this type of involuntary dyskinetic movement disorder produced by long-term CPZ administration is discussed. 45 references. (Author abstract)

189219 Yamamoto, Takashi; Kawamura, Yojiro. Department of Oral Physiology, Dental School, Osaka University, 32 Joancho, Kitaku, Osaka, Japan **Chloroform responses of the chorda tympani nerve in the rat.** Physiology & Behavior. 13(2):245-250, 1974.

Electrophysiological analysis of the chorda tympani nerve response to saturated chloroform solution was performed in the rat, and the results were compared to those of the sucrose response. The chloroform response was characterized by a transient response, and it lacked an offtype response to the water rinse of the tongue. Treatment of the tongue with 0.1M anionic detergent and HgCl2 produced the same effects on the chloroform and sucrose responses. However, the effects of some metallic ions on response to chloroform were different form those on the sucrose response. Additive effect of sucrose and chloroform was rather smaller than the summation expected by doubling of the responses of sucrose and chloroform. The fibers which showed the offtype discharges also always responded to chloroform. These results suggest that sucrose and chloroform combine to the different loci within the same taste receptor macromolecule. 10 references. (Author abstract modified)

189381 Seiser, Richard L.; Houser, Vincent P. Psychotropic Drug Laboratory, VA Hospital, Perry Point, MD 21902 **Effects**

of scopolamine methylbromide on shock-induced gastric lesions in the unrestrained rat. Physiology & Behavior. 13(1):147-151, 1974.

The effects of scopolamine methylbromide on shock induced gastric lesions in the unrestrained rat were studied. Gastric lesions were produced in unrestrained rats subjected to a 6 hr shock stress session. A perch contingent yoked design compared the degree of gastric pathology exhibited in animals subjected to an avoidance - avoidance conflict, with yoked animals receiving equivalent amounts of noncontingent shock. There were no differences in the amount of gastric lesion formation produced by these two procedures. Scopolamine methylbromide significantly decreased ulcer development (i.e.,percentage of animals exhibiting pathology, number of lesions per animal and severity of lesioning) in all groups tested. 19 references. (Author abstract)

189390 Berkowitz, Barry A.; Tarver, James J.; Spector, Sydney. Roche Institute of Molecular Biology, Nutley, NJ 07110 **Control of norepinephrine synthesis in blood vessels and the effects of monoamine oxidase inhibition.** Journal of Pharmacology and Experimental Therapeutics. 190(1):21-29, 1974.

End product regulation of norepinephrine (NE) synthesis in the vasculature was examined. NE inhibits vascular tyrosine hydroxylase both in vivo and in vitro. However, in the intact guinea pig, elevation of NE levels after pargyline resulted in a 70% to 80% inhibition of NE synthesis in the heart, aorta and mesenteric vein whereas the synthesis of NE in the mesenteric artery was inhibited only 40% or less. It is suggested that in the heart, aorta and mesenteric vein, the NE storage capacity is rapidly filled after monoamine oxidase inhibition and that NE which is not bound readily inhibits tyrosine hydroxylase. In the mesenteric artery and presumably other densely innervated arteries where the tyrosine hydroxylase activity is very high, the larger reserve NE storage capacity limits the amount of catecholamine which can be achieved in the immediate vicinity of tyrosine hydroxylase. The result is that feedback inhibition by end product and the effects of pargyline vary in different parts of the cardiovascular system with arteries being the least sensitive. 35 references. (Author abstract)

189394 Greenberg, Stanley; Wilson, William R.; Howard, Linda. Department of Physiology, College of Medicine, University of Michigan, Ann Arbor, MI 48104 **Mechanism of the vasoconstrictor action of prostaglandin B.** Journal of Pharmacology and Experimental Therapeutics. 190(1):59-69, 1974.

The mechanism of prostaglandin B induced vasoconstriction was studied in the dog hindpaw perfused at constant flow. Intraarterial infusions of PGB2 and PGB1 produced vasoconstriction. Depletion of catecholamines by reserpine decreased PGB induced vasconstriction. PGB2 was a vasodilator in reserpine pretreated animals. Atropine and decamethonium did not affect PGB induced vasoconstriction. Cocaine enhanced PGB1 and PGB2 induced vasconstriction, whereas blockade of sodium conductance and neuronal depolarization with tetrodotoxin reduced vasoconstrictor responses to PGB1 and PGB2. Infusions of l-norepinephrine in reserpine pretreated animals restored the responses to intraarterial tyramine but not those to sympathetic nerve stimulation, PGB1 and PGB2. Since catecholamine depletion and blockade of depolarization reduced pressor responses to PGB compounds and since depletion of cytoplasmic norepinephrine stores did not restore PGB induced vasoconstriction, the data show that PGB compounds release norepinephrine from the granular store by a mechanism dependent on depolarization. 31 references. (Author abstract)

189395 Greenberg, Stanley; Howard, Linda; Engelbrecht, James; Wilson, William R. Department of Physiology, College of Medicine, University of Michigan, Ann Arbor, MI 48104 **Effects of prostaglandins B1 and B2 on vasoconstrictor responses of the canine hindpaw.** Journal of Pharmacology and Experimental Therapeutics. 190(1):70-76, 1974.

The effects of prostaglandin B1 (PGB1) and prostaglandin B2 (PGB2) on the responses of the canine perfused hindpaw to adrenergic nerve stimulation and the pressor responses to intraarterial injections of tyramine and norepinephrine were studied in 32 dogs. Intraarterial infusions of PGB2 produced concentration dependent increases in the pressor responses to adrenergic nerve stimulation. The pressor responses of the denervated paw to tyramine and norepinephrine were not altered during infusions of PGB2. Intraarterial infusions of PGB1 produced effects similar to that of PGB2 but were less potent. Since PGB2 and PGB1 enhance the pressor responses to nerve stimulation, but not those to tyramine or norepinephrine, the data are consistent with the conclusion that PGB compounds facilitate release of the neurotransmitter from the norepinephrine pool utilized by the nerve action potential. 36 references. (Author abstract modified)

189396 Pollard, Helene; Bischoff, Serge; Schwartz, Jean-Charles. Unite de Neurobiologie, 2 Ter, Rue d'Alesia, Paris, 75014, France **Turnover of histamine in rat brain and its decrease under barbiturate anesthesia.** Journal of Pharmacology and Experimental Therapeutics. 190(1):88-99, 1974.

The turnover of histamine in rat brain and its decrease under barbiturate anesthesia was examined. After an intraventricular injection of 3H-L-histidine (3H-His), levels of 3H-histamine (3H-HA) in rat brain were found to peak at 1 hour and then to decline monoexponentially. A major portion of 3H-HA was present in the crude mitochondrial fraction, as reported for endogenous HA. By making several assumptions, HA turnover was tentatively evaluated by applying steady state kinetics of the fluctuations of 3H-HA and 3H-His levels up to 30 minutes. Measurement of 3H-methylhistamine levels after intraventricular injection of 3H-His, both in saline and pargyline treated rats, confirmed that the catabolism of endogenous HA occurs, like that of the exogenous amine, mainly if not solely by methylation. The subcellular distribution of 3H-methylhistamine between primary fractions was parallel to that of 3H-HA. In rats anesthetized with thiopental (penthiobarbital), there was a rapid and marked reduction in HA turnover, evidenced by a decrease both in the synthesis and disappearance of 3H-HA, without alteration in the endogenous levels of HA or L-His. 42 references. (Author abstract modified)

189397 Chiueh, C. C.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Effects of alpha-methyltyrosine on d-amphetamine-induced release of endogenously synthesized and exogenously administered catecholamines from the cat brain in vivo.** Journal of Pharmacology and Experimental Therapeutics. 190(1):100-108, 1974.

A cerebroventricular perfusing technique was utilized to measure the efflux of 3H-catecholamines from cat brain. The presence of alpha-methyltyrosine (MT) in the cerebrospinal fluid (CSF) did not alter the amphetamine induced response. Amphetamine also increased the efflux of 3H-catecholamines, which consisted almost entirely of 3H-dopamine after brain stores were labeled by an intraventricular infusion of 3H-tyrosine. The addition of MT to the CSF prior to and during the infusion of 3H-tyrosine blocked the synthesis of 3H-

catecholamines so that the subsequent administration of amphetamine failed to increase the efflux of these amines. However, if brain stores of catecholamines were first labeled by the infusion of 3H-tyrosine, the subsequent addition of MT to the CSF did not alter the amphetamine induced efflux of 3H-catecholamines from the brain. The intraventricular infusion of MT blocks the synthesis of brain catecholamines, but it does not interfere with the ability of amphetamine to release these amines. 22 references. (Author abstract modified)

189398 Green, Thomas K.; Harvey, John A. Long Beach VA Hospital, Long Beach, CA 90801 **Enhancement of amphetamine action after interruption of ascending serotonergic pathways.** Journal of Pharmacology and Experimental Therapeutics. 190(1):109-117, 1974.

The enhancement of amphetamine action after interruption of ascending serotonergic pathways was studied in the rat. Large lesions, producing 60% to 90% destruction of the medial forebrain bundle (MFB) and a 60% to 84% decrease in telencephalic content of serotonin, also produced a three fold enhancement of amphetamine action as measured by increased rates of responding on a variable interval 60 second schedule of reinforcement. These lesions had no effect on the action of chlorpromazine. Smaller lesions, producing 10% to 50% destruction of the MFB and a 1% to 59% decrease in serotonin, had no effect on amphetamine action. Lesions in the septal area, central gray, dorsomedial tegmentum or ventrolateral tegmentum produced only small decreases in serotonin and had no effect on amphetamine action. It was concluded that the serotonergic system plays an important role in determining the magnitude of amphetamine effects on behavior. 35 references. (Author abstract modified)

189400 Seeman, P.; Staiman, A.; Chau-Wong, M. Pharmacology Department, University of Toronto, Toronto 5, Canada **The nerve impulse-blocking actions of tranquilizers and the binding of neuroleptics to synaptosome membranes.** Journal of Pharmacology and Experimental Therapeutics. 190(1):123-130, 1974.

In order to test the presynaptic coupling blockade hypothesis of neuroleptic drug action, we measured the conduction blocking concentrations for phenothiazines and butyrophenones using rat phrenic nerve. The concentrations required to block the rat sciatic nerve were about 10 fold higher than those for rat phrenic nerve. The synaptosome membrane/buffer partition coefficients were 18.8for promethazine, 295 for imipramine, 1700 for chlorpromazine, 8500 for thioridazine 200 for haloperidol and 80 for trifluperidol. Calcium displaced the neuroleptics from the synaptosome membranes. The blocking potencies correlated with the daily dosage used to control acute schizophrenia and with the octanol/water partition coefficients. Since the threshold blocking concentrations are in the same range as those found in the patient's plasma water, it is suggested that presynaptic blockade of coupling (between impulse and dopamine release) may play a role in the antipsychotic and extrapyramidal actions of neuroleptics. 40 references. (Author abstract modified)

189401 Seeman, P.; Lee, T. Pharmacology Department, University of Toronto, Toronto 5, Canada **The dopamine-releasing actions of neuroleptics and ethanol.** Journal of Pharmacology and Experimental Therapeutics. 190(1):131-140, 1974.

The dopamine releasing actions of neuroleptics and of ethanol were studied on rat caudate synaptosome fractions (unpurified) which had been loaded with 3H-dopamine in vitro. The threshold concentrations above which chlorpromazine, haloperidol, reserpine phosphate, pimozide and benztropine enhanced the spontaneous release of dopamine from synaptosomes were determined. The threshold concentrations above which the uptake of dopamine was inhibited were generally about 5 to 10 times higher. The threshold concentration above which ethanol potentiated the spontaneous release of dopamine from the synaptosome fraction was 0.05 M or 0.23g/100 ml. This concentration produces general anesthesia in the human. It is postulated that the side-effects of neuroleptic induced parkinsonism and tardive dyskinesia are based on the impulse blocking and dopamine releasing actions of the neuroleptics, respectively. 48 references. (Author abstract modified)

189407 Colasanti, Brenda K.; Craig, Charles R.; Hartman, Elizabeth R. Department of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Differential effects of pentylenetetrazol on REM sleep in naive and cobalt-epileptic rats.** Psychopharmacologia (Berlin). 37(2):151-157, 1974.

The differential effects of pentylenetetrazol on rapid eye movement (REM) sleep were studied in naive and cobalt epileptic rats. Administration of pentylenetetrazol at a dose of 15mg/kg every 15 min until the appearance of generalized convulsions resulted in the lowering of the chemical seizure threshold expected for the cobalt treated rats, with only two injections of the drug required in contrast to the three to four injections needed for the control rats. Analysis of the electroencephalogram (EEG) recordings collected over the 24 h period after the first injection revealed the presence of a more pronounced suppression of rapid eye movement (REM) sleep in the cobalt epileptic rats. This effect was found to be due to a reduction in the total number of REM sleep episodes, while the duration of the individual episodes remained unchanged. The latencies to REM onset in these rats were markedly reduced. These results in a chronic seizure model further support the usefulness of cobalt experimental epilepsy in the rat for the study of human seizure disorders in comparison with acute seizure models. 24 references. (Author abstract modified)

189425 Lober, Clifford Warren. Duke University Medical Center, Durham, NC 27706 **Case against the use of d-tubocurarine in operant studies of the cardiovascular system.** Perceptual and Motor Skills. 38(3,Part2):1287-1292, 1974.

The case against the use of d-tubocurarine in operant studies of the cardiovascular system is presented. After reviewing evidence showing a high degree of integration between the autonomic and somatic systems, it is shown that d-tubocurarine alters both the central and peripheral perception and response patterns. Many of the observations made upon curarized animals can be explained by a central motor theory. Experimental use of curarine is hindered by the release of histamine in response to administration of curarine. Among other artifacts, curarine induced release of histamine caused a progressive decrease of pulmonary compliance. When artificial respiration is given to curarized animals, the use of positive pressure ventilation and failure to monitor pulmonary gases are further sources of artifacts. 47 references. (Author abstract modified)

189513 Chesher, G. B.; Jackson, D. M. Department of Pharmacology, University of Sydney, Sydney, N.S.W 2006, Australia **Anticonvulsant effects of cannabinols in mice: drug interactions with cannabinoids and cannabinoid interactions with phenytoin.** Psychopharmacologia (Berlin). 37(3):255-264, 1974.

The anticonvulsant activity of orally administered delta 9-tetrahydrocannabinol (THC), delta 8-THC, cannabidiol (CBD) and cannabinol (CBN) was tested in mice utilizing electroshock and chemoshock methods. In doses tested THC afforded no protection to mice from chemoshock seizures and was effective against electroshock only in high doses. CBD and CBN were without effect in both tests. An interaction between cannbinoids was apparent when all three were administered simultaneously because this combination produced a significant reduction in the duration of the hind limb extensor phase of the electroshock seizures. The administration of THC significantly potentiated the anticonvulsant effectiveness of phenytoin against electroshock seizures and this effect was further potentiated by the concurrent administration of CBD. Neither within cannabinoid interaction nor cannabinoid potentiation of phenobarbitone effectiveness could be demonstrated in chemoshock tests. 25 references. (Author abstract modified)

189567 Erdmann, Erland; Schoner, Wilhelm. Institut fur Biochemie und Endokrinologie, D-6300 Giessen, Frankfurter Str. 112, Germany **Ouabain-receptor interactions in (Na+ + K+)-ATPase preparations.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(4):335-356, 1974.

Dissociation constants (Kp) of the drug receptor complexes of 28 different cardiac glycosides have been determined either with 03H0 labelled cardioactive steroids or from displacement of (3H) ouabain with unlabelled cardiac glycosides from the receptor. There is only one single type of cardiac glycoside receptor. Structure affinity relationship of the different cardiac glycosides indicate that cardiac glycosides are recognized from interactions with: 1) the unsaturated lactone group; 2) the steroid nucleus with a cis-configuration of the A:B ring junction; and 3) the sugar component. Diphenylhydantoin displaces cardiac glycosides from the receptor, and so does prednison-3,20-bisguanylhydrazone. The cardiac glycoside receptor concentration increases proportionally with sodium + potassium (Na + K) activated adenosine triphosphatase (ATPase) activity. Occupation of the cardiac glycoside receptor results in a proportional inhibition of (Na + K) ATPase activity. 63 references. (Author abstract modified)

189568 Montel, H.; Starke, K.; Weber, F. Pharmakologisches Institut, Klinikum Essen, D-4300 Essen, Hufelandstrasse 55, Germany **Influence of morphine and naloxone on the release of noradrenaline from rat brain cortex slices.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(4):357-369, 1974.

In slices of rat brain cortex preincubated with (-)-3H-noradrenaline, the influence of morphine and naloxone on the efflux of tritium was investigated. The spontaneous outflow of tritium was not changed by small doses morphine and by naloxone, but was accelerated by larger doses morphine. Electrical field stimulation augmented tritium outflow. The overflow evoked per pulse decreased as the frequency of stimulation was increased from 0.3to 3 Hz, but remained approximately constant when it was further increased to 10 Hz. Naloxone did not change the response to stimulation. In the presence of naloxone, morphine did not diminish, and morphine even enhanced the stimulation induced overflow of tritium. The inhibitory effect of morphine was not reduced, after tyrosine hydroxylase had been blocked by alpha-methyltyrosine-methyl-ester. It is concluded that morphine through an action on specific opiate receptors inhibits the release of transmitter from cerebrocortical noradrenergic neurons evoked by nerve impulses. 38 references. (Author abstract modified)

189569 Montel, H.; Starke, K.; Weber, F. Pharmakologisches Institut, Klinikum Essen, D-4300 Essen, Hufelandstrasse 55, Germany **Influence of fentanyl, levorphanol and pethidine on the release of noradrenaline from rat brain cortex slices.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(4):371-377, 1974.

In slices of rat brain cortex preincubated with (-)-3H-noradrenaline, the influence of fentanyl, levorphanol and pethidine on the efflux of tritium was investigated. The spontaneous outflow of tritium was not changed by low, and was accelerated by high concentrations of the drugs. The overflow of tritium evoked by electrical stimulation at 3 Hz was diminished by fentanyl and by small doses levorphanol, but was augmented by larger doses levorphanol. Naloxone prevented the inhibitory effect of fentanyl and levorphanol. In contrast to fentanyl and levorphanol, pethidine did not decrease, but greatly increased the stimulation induced overflow of tritium. The increase was abolished, and the stimulation evoked overflow slightly reduced, after the reuptake of noradrenaline had been blocked by cocaine. It is concluded that fentanyl, levorphanol and pethidine share with morphine the ability to inhibit the release of transmitter from cerebrocortical noradrenaline neurons evoked by nerve impulses. 7 references. (Author abstract)

189571 Anden, Nils-Erik; Magnusson, Tor; Stock, Gunter. Department of Pharmacology, University of Goteburg, Fack, S-400 33 Goteburg 33, Sweden **Effect of anaesthetic agents on the synthesis and disappearance of brain dopamine normally and after haloperidol, KCl or axotomy.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(4):409-418, 1974.

The synthesis of dopamine was determined as the accumulation of dopa after dopa carboxylase inhibition. The release of dopamine was determined as the disappearance of the amine after treatment with the tyrosine hydroxylase inhibitor alpha-mehtyltyrosine. These processes were not significantly changed in the rat brain by pentobarbital sodium anaesthesia or by 10 min halothane anesthesia. The accelerations of the dopamine synthesis and release after treatment with haloperidol were markedly reduced during pentobarbital, but not halothane anesthesia. Anesthesia with pentobarbital did not affect the increased synthesis and release of dopamine observed when the dopaminergic nerve terminals were depolarized by local treatment with potassium chloride. The increases in dopamine synthesis and concentration after axotomy were similar whether the operation was performed during pentobarbital or halothane anesthesia. It is suggested that the selective reduction of the haloperidol induced effects by pentobarbital may be due to interference with a neuronal feedback loop. 27 references. (Author abstract)

189586 Loh, Horace H.; Hitzemann, Robert J. Langley Porter Neuropsychiatric Institute, San Francisco, CA 94122 **Effect of morphine on the turnover and synthesis of (Leu-3H)-protein and (Ch-14C)-phosphatidylcholine in discrete regions of the rat brain.** Biochemical Pharmacology (Oxford). 23(12):1753-1765, 1974.

The effect of acute and chronic morphine treatment on the synthesis and turnover of 3H-leucine labeled protein and 14C-choline labeled phosphatidylcholine was measured in discrete regions of the rat brain. Chronic morphine treatment had the following effects on turnover: in the crude mitochondrial fraction of all brain regions studied, the turnover of 3H-protein was decreased; microsomal 3H-protein turnover was increased in the cerebellum and hypothalamus and decreased in the cor-

tex; the turnover of 14C-phosphatidylcholine was increased in the crude mitochondrial faction of the brainstem, hypothalamus and diencephalon, but decreased in the cortex; in the microsomal fraction, the turnover of 14C-phosphatidylcholine was decreased in the cortex, brainstem and caudate nucleus, but increased in the diencephalon. Acute morphine treatment decreased 14C-phosphatidylcholine synthesis in the cortex and cerebellum, but increased synthesis in the hypothalamus and diencephalon. Acute morphine treatment decreased 3H-protein synthesis in the cotex and diencephalon, but increased 3H-protein synthesis in the hypothalamus and caudate nuclesu. The relevance of these findings to current theories to narcotic tolerance and physical dependence development is discussed. 48 references. (Author abstract)

189589 Maickel, R. P.; Fedynskyj, N. M.; Potter, W. Z.; Manian, A. A. Department of Pharmacology, Indiana University, Bloomington, IN 47401 **Tissue localization of 7- and 8-hydroxychlorpromazines.** Toxicology and Applied Pharmacology. 28(1):8-17, 1974.

The time course of physiological disposition of 3H-labeled 7-hydroxychloropromazine and 8-hydroxychlorpromazine were examined in rats after a single dosage, and the accumulation of each compound has been studied after 6, 14 and 28 doses on a bid schedule. The 8-hydroxycompound decays at a slower rate and shows a greater degree of accumulation on repeated dosage than does the 7-hydroxychlorpromazine. Both compounds enter the brain (the 7-hydroxy to a greater extent) and distribute uniformly, with no significant overt behavioral effects. Both compounds caused significant liver and kidney damage as demonstrated by histological evaluation. 18 references. (Author abstract)

189590 Jakubovic, A.; Tait, R. M.; McGeer, P. L. Department of Psychiatry, University of British Columbia, Vancouver 8, British Columbia, Canada **Excretion of THC and its metabolites in ewes' milk.** Toxicology and Applied Pharmacology. 28(1):38-43, 1974.

The excretion of delta9-tetrahydrocannabinol (THC) and its metabolites in ewes' milk was studied. After single iv injections of either 0.02mg/kg or 1mg/kg of labeled THC, to lactating ewes, radioactivity was detected in the milk at all subsequent time intervals tested. Radioactivity was found in unchanged THC as well as in various unidentified metabolites. Only about 15% of the administered radioactivity was excreted by the ewes in the first 48 hr; most of this was in the urine and feces. Radioactivity appeared in the feces and urine of a lamb suckling milk from a ewe injected with THC, indicating transfer of THC and its metabolites via the milk. The results indicate slow elimination of THC, and show that milk is an additional route of excretion. 12 references. (Author abstract)

189591 Borowitz, J. L. Department of Pharmacology and Toxicology, Purdue University, West Lafayette, IN 47907 **Mechanism of adrenal catecholamine release by divalent mercury.** Toxicology and Applied Pharmacology. 28(1):82-87, 1974.

The mechanism of adrenal catecholamine release by divalent mercury was studied. The decline of mercury induced catecholamine release from isolated perfused bovine adrenals is biphasic when mercury concentrations of .00009M or above are used. After initiation of catecholamine release by .00003M mercury, the response declines in a monophasic manner which corresponds to the first phase of decline seen after exposure of adrenals to higher mercury concentrations. Neither phase is altered by .005M magnesium, but the second phase is eliminated when calcium is omitted from the medium. 45Ca washout from labeled adrenals is decreased by .0002 Hg2+ but is not affected by .00003M Hg2+. Acetylcholine and mercury interact approximately in an additive manner in releasing adrenal catecholamines. The initial phase of mercury induced adrenal catecholamine release may be due to amine displacement by the mercury ion. The secondary phase of adrenal catecholamine release probably involves alteration of membrane structures by mercury. 7 references. (Author abstract)

189597 Thompson, Jeremy H.; Su, Che; Shih, Jean C.; Aures, Dorothea; Choi, Leslie; Butcher, Sherrel; Loskota, William S.; Simon, Marcia; Silva, Douglas. Department of Pharmacology and Experimental Therapeutics, UCLA Schools of Medicine and Dentistry, Los Angeles, CA 90024 **Effects of chronic nicotine administration and age on various neurotransmitters and associated enzymes in male Fischer-344 rats.** Toxicology and Applied Pharmacology. 27(1):41-59, 1974.

The acute, subacute and chronic effects of nicotine were studied in male Fischer-344 rats. Nicotine pretreatment did not significantly alter 5-hydroxytryptamine (5-HT) or norepinephrine (NE) concentrations in a variety of tissues, nor whole brain choline (Cho), acetylcholine (ACh) and acetylcholinesterase activity. Gamma-aminobutyric acid concentrations in eight brain areas were all higher after chronic nicotine administration, but histamine (HM) concentrations were variably affected in a variety of tissues. The uptake of 5-HT into the heart and gastrointestinal mucosa, and of NE into the heart and aorta, was not affected by nicotine treatment. However, uptake of NE into synaptosomes prepared from an homogenate of whole brain was depressed. Urinary 5-hydroxyindoleacetic acid (5-HIAA) excretion was significantly higher in nicotine treated rats compared control animals both during ad libitum feeding and during food deprivation. In addition, urinary 5-HIAA excretion was significantly higher in nicotine treated rats with food deprivation compared to ad libitum feeding. 64 references. (Author abstract modified)

189599 Luthra, Yugal K.; Rosenkrantz, Harris. Department of Biology, Clark University, Worcester, MA 01610 **Cannabinoids: neurochemical aspects after oral chronic administration to rats.** Toxicology and Applied Pharmacology. 27(1):158-168, 1974.

The neurochemical aspects of delta9-tetrahydrocannabinol (THC) after oral chronic administration to rats were examined. Male and female Fischer rats were treated orally with THC doses or with crude marihuana extract for 28 or 91 consecutive days. Significant decreases were obtained for protein, ribonucleic acid (RNA) and acetylcholinesterase activity at 28 days and monoamine oxidase at 91 days. No changes in total lipids, glycolipids or cholesterol concentrations were observed. The neurochemical alterations coincided with behavioral symptoms of hyperactivity and convulsive activity. Both neurotoxicity and neurochemical changes were partially reversed after the longer interval of treatment. 45 references. (Author abstract modified)

189602 Stadler, H.; Lloyd, K. G.; Bartholini, G. Department of Psychopharmacology, Clarke Institute of Psychiatry, 250 College St., Toronto, Canada **Dopaminergic inhibition of striatal cholinergic neurons: synergistic blocking action of gamma-butyrolactone and neuroleptic drugs.** Archives of Pharmacology (Berlin). 283(2):129-134, 1974.

The effect of drugs administered on the release of acetylcholine (ACh) within the caudate nucleus' perfused by means of push pull cannula was studied in the gallamine im-

mobilized cat. The antipsychotic compound clozapine (a dopamine receptor blocking agent) markedly increased the ACh output. Combination of gamma-butyrolactone with clozapine caused an increase of ACh output similar to that observed after clozapine. Similar results were obtained with chlorpromazine. Results suggest that cholinergic neurons in the striatum are under an inhibitory dopaminergic influence. The lack of effect on ACh output of relatively low doses of neuroleptics is explained by a partial dopamine receptor blockade which is surmounted by the feedback activation of dopaminergic neurons. Impairment of this activation by gamma-butyrolactone is likely to result in a further diminution of dopamine at the receptors, leading to a disinhibition of cholinergic neurons. 20 references. (Author abstract)

189604 Bonisch, H.; Trendelenburg, U. Institut fur Pharmakologie und Toxikologie der Universitat, D-8700 Wurzburg, Koellikerstrasse 1, Germany **Extraneuronal removal, accumulation and O-methylation of isoprenaline in the perfused heart.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(2):191-218, 1974.

Extraneuronal removal, accumulation and O-methylation of isoprenaline were examined in the perfused rat and guinea pig hearts. Isolated rat and guinea pig hearts were perfused with isoprenaline or H(+)-isoprenaline, a — catecholamine which is taken up by extraneuronal mechanisms only. From measurements of the arteriovenous difference the rate of removal of the amine from the perfusion fluid was measured; in addition, the rate of appearance of its metabolite (3-O-methyl-3H-isoprenaline; 3H-OMI) was determined in the venous effluent as well as the accumulation of 3H-isoprenaline and 3H-OMI in the heart. The removal of 3H-isoprenaline from the perfusion fluid declined biphasically with time; after an initial rapid decline the rate of removal approached steady state levels within about 30 min. After block of COMT the second phase of decline approached zero. When COMT was intact, 3H-OMI appeared in the venous effluent, first at a rapidly increasing rate, from the 9th minute of perfusion onward at a steady rate which was identical with the steady state rate of removal of 3H-isoprenaline. The accumulation of 3H-isoprenaline in the heart reached a steady level within about 30 min; block of COMT increased the time required for approach to steady levels and increased the accumulation of 3H-isoprenaline in the rat (but not in the guinea pig) heart. 25 references. (Author abstract modified)

189605 Lullmann-Rauch, Renate. Anatomisches Institut der Universitat, D-2300 Kiel, Olshausenstrasse, Germany **Lipidosis-like alterations in dorsal root ganglion cells of rats treated with tricyclic antidepressants.** Archives of Pharmacology (Berlin). 283(2):219-222, 1974.

Lipidosis like alterations were examined in dorsal root ganglion cells of rats treated with tricyclic antidepressants. Prolonged treatment of rats with high doses of the tricyclic antidepressants iprindole, clomipramine, or 1-chloramitriptyline induced the formation of lamellated and crystalloid cytoplasmic inclusion bodies within dorsal root ganglion cells. The ultrastructural observations, which are compatible with the concept of a drug induced generalized phospholipidosis, indicate that under experimental conditions also nerve cells can be affected by this type of drug side-effect. 8 references. (Author abstract)

189608 Izquierdo, Ivan. Departamento de Fisiologia, Farmacologia e Biofisica, Universidade Federal de Rio Grande do Sul, Porto Alegre, RS Brazil **Effect of anticonvulsant drugs on the number of afferent stimuli needed to cause a hippocampal seizure discharge.** Pharmacology. 11(3):146-150, 1974.

The effect of anticonvulsant drugs on the number of afferent stimuli needed to cause a hippocampal seizure discharge was examined. The anticonvulsant drugs, cannabidiol, phenobarbital, diphenylhydantoin and trimethadione, raise the number of stimuli at a 10 sec rate to the fornix needed to cause a hippocampal seizure discharge. The possible value of this test as a method for the assay of antiepileptic agents is analyzed. 17 references. (Author abstract)

189609 Tannhauser, Mario; Izquierdo, Ivan. Departamento de Fisiologia, Farmacologia e Bifisica, Universidade Federal de Rio Grande do Sul, Porto Alegre, Brazil **Effect of seizures and anticonvulsant agents on hippocampal RNA concentration.** Pharmacology. 11(3):139-145, 1974.

The effects of seizures and anticonvulsant agents on hippocampal riboneucleic acid (RNA) concentrations were studied. Epileptogenic stimulation of the fornix during 25 min caused a fall of total hippocampal RNA concentration in rats. This fall was prevented by the preadministration of phenobarbital, trimethadione, diphenylhydantoin or cannabidiol, which, however, were unable to block seizure discharges in most cases. The administration of any of these anticonvulsant agents to awake animals had no effect on neocortical and hippocampal RNA levels. Generalized convulsions provoked in awake animals by metrazol, electroshock or hyponatremia also had no effect on neocortical or hippocampal RNA. 17 references. (Author abstract)

189611 Lidbrink, Peter; Corrodi, Hans; Fuxe, Kjell. Department of Histology, Karolinska Institutet, Stockholm, Sweden **Benzodiazepines and barbiturates: turnover changes in central 5-hydroxytryptamine pathways.** European Journal of Pharmacology (Amsterdam). 26(1):35-40, 1974.

The effect of chlordiazepoxide, diazepam and phenobarbitone on 5-hydroxytryptamine turnover in the cortex cerebri as compared to the rest of the brain was studied in rats using biochemical determinations of 5-hydroxytryptamine. Chlordiazepoxide and diazepam reduced the turnover of 5-hydroxytryptamine in the cortex cerebri, whereas no change was found in the rest of the brain. Lower doses of chlordiazepoxide were ineffective. Phenobarbitone reduced the turnover of 5-hydroxytryptamine both in the cortex cerebri and in the rest of the brain. Lower doses were without effect. The doses of the various drugs which yielded an effect on the depletion of 5-hydroxytryptamine caused pronounced sedation. It is suggested that chlordiazepoxide and diazepam in sedative doses decrease the turnover of 5-hydroxytryptamine in the 5-hydroxytryptamine pathway to the cortex cerebri whereas phenobarbitone causes a generalized decrease in turnover in the brain 5-hydroxytryptamine neurons. 28 references. (Author abstract modified)

189616 Miller, R. J.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge CB2 2QD, England **Stimulation of a dopamine-sensitive adenylate cyclase in homogenates of rat striatum by a metabolite of piribedil (ET 495).** Archives of Pharmacology (Berlin). 282(2):213-216, 1974.

The stimulation of a dopamine sensitive adenylate cyclase in homogenates of rat striatum by a metabolite of piribedil (ET 495) is reported. The addition of dopamine (1-100micromolar) to homogenates of rat striatum incubated with adenosine triphosphate (ATP) evoked a 120% increase in the rate of

cyclic 3'5' adenosine monophosphate (cyclic AMP) production. The effects of added dopamine were mimicked by the addition of the compound S 584 (1-3,4-(dihydroxybenzyl)-4-(2-pyrimidinyl) piperazine), a catechol metabolite of the dopaminergic stimulant drug piribedil (ET 495). The latter substance was itself inactive in this system at these concentrations. The stimulation of cyclic AMP production by dopamine and by S 584 was potently inhibited by the dopamine antagonist drugs chlorpromazine and spiroperidol. It is possible that the dopaminergic effects elicited by piribedil may be mediated through the active metabolite S 584. 10 references. (Author abstract)

189750 Davies, J.; Watkins, J. C. Dept. of Pharmacology, John Curtin School of Medical Research, Australian National University, Canberra, Australia **The action of beta-phenyl-GABA derivatives on neurones of the cat cerebral cortex.** Brain Research (Amsterdam). 70(3):501-505, 1974.

The action of beta-p-chlorophenyl-GABA (B-p-CPG), a new centrally acting muscle relaxant, and other beta-aryl-GABA derivatives were compared with those of GABA on single feline cerebral cortical neurons. All the beta-phenyl-GABA derivatives reversibly reduced the chemically induced firing rate of cortical neurons. B-p-CPG was most effective, having about 0.7times the activity of GABA. The duration of the depressant action of all the beta-phenyl-GABA derivatives was considerably longer than that of GABA following ejection from micropipettes. The depressant action of B-p-CPG was not antagonized by bicuculline which suggests that the B-aryl-GABA derivatives do not exert a GABA like action on cortical neurons. Attention is drawn to the structural similarity of the beta-phenyl-GABA derivatives and those of the catecholamines. 7 references. (Author abstract modified)

189752 Turner, A. J.; Ponzio, F.; Algeri, S. Department of Biochemistry, University of Leeds, 9 Hyde Terrace, Leeds LS 2, 9LS, England **Dihydropteridine reductase in rat brain: regional distribution and the effect of catecholamine-depleting drugs.** Brain Research (Amsterdam). 70(3):553-558, 1974.

To investigate the possible relationship between dihydropteridine reductase (DHPR) activity in brain and the control of catecholamine or indoleamine synthesis, the regional localization of DHPR in rat brain and the effects of catecholamine depleting drugs upon its activity were examined. Findings on regional distribution of DHPR in rat brain indicate that highest activity is observed in the brainstem, and distribution parallels neither that of tyrosine hydroxylase nor tryptophan hydroxylase. Although treatment with 6-hydroxydopamine caused a significant reduction in brain noradrenaline and dopamine content, and in tyrosine hydroxylase activity, no change in the activity of DHPR was observed. The high activity of DHPR in brain and its general distribution in neuronal as well as other tissues suggests that the rate of production of reduced pterine may not be a limiting factor in amine synthesis. 18 references.

189832 Levy, Richard A.; Anderson, Edmund G. Dept. of Pharmacology, College of Medicine, Univ. of Illinois at the Medical Center, Chicago, IL 60680 **The role of gamma-aminobutyric acid as a mediator of positive dorsal root potentials.** Brain Research (Amsterdam). 76(1):71-82, 1974.

The role of gamma-aminobutyric acid (GABA) as a mediator of positive dorsal root potentials was investigated in the cat. A diphasic response consisting of a negative going, followed by a positive going dorsal root potential (DRP) was evoked in L6 or L7 dorsal rootlets of unanesthetized spinal cats by 10 times group I threshold stimulation of the gastrocnemius - soleus muscle nerve. The administration of bicuculline reversibly abolished first the negative, then the positive DRP. A selective action against negative DRP was also observed after picrotoxin administration. Semicarbazide induced a gradual diminution and often abolition of both DRPs over a 3 h period. Suppression of the positive DRP by agents which block the receptor attachment and synthesis of GABA suggests that GABA was a transmitter in the pathway(s) mediating primary afferent hyperpolarization. The possibility that GABA synapses occur in each of two separate pathways leading to the afferent terminal is discussed. 56 references. (Author abstract modified)

189843 Izumi, Kanji; Igisu, Hideki; Fukuda, Takeo. Dept. of Neurology, Neurological Institute, Kyushu University, Fukuoka 812, Japan **Suppression of seizures by taurine -- specific or non-specific?** Brain Research (Amsterdam). 76(1):171-173, 1974.

The possibility that taurine may possess a nonspecific ability to depress epileptic seizure activity was investigated. Since taurine is known to relieve seizures induced by agents acting on the sodium pump, its effect on seizures induced by pentylenetetrazol (PTZ), which is believed not to affect this activity, was examined to determine taurine's specificity. It was found that iv injected taurine reduced PTZ induced seizures in a dose dependent and time dependent manner, demonstrating the nonspecific anticonvulsant action of taurine and supporting the view that it may have a role as an inhibitory neurotransmitter in the CNS. 10 references.

189855 Spehlmann, Rainer; Downes, Kathleen. VA Research Hospital, Chicago, IL 60611 **The effects of acetylcholine and of synaptic stimulation on the sensorimotor cortex of cats. I. Neuronal responses to stimulation of the reticular formation.** Brain Research (Amsterdam). 74(2):229-242, 1974.

The relationship between the effects of acetylcholine on single neurons in the sensorimotor cortex of cats and the synaptic transmission of impulses to these neurons from the mesencephalic reticular formation was examined. The iontophoretic application of acetylcholine from extracellular multibarreled micropipettes increased the firing rate of about one third of the 103 neurons studied and decreased it in about one sixth of them. Repetitive electrical stimulation of the reticular formation produced unsustained, multiphasic or sustained changes of firing in many neurons; initial excitation was more common than initial depression. Many neurons reacted by excitation to both acetylcholine and reticular stimulation but some neurons were depressed by acetylcholine and excited by reticular stimulation and still others were depressed by both agents. Atropine and scopolamine, which antagonized the effects of acetylcholine, also blocked the excitatory responses to reticular stimulation in some acetylcholine excited neurons. The depressant effects of reticular stimulation were not antagonized by these agents. Results support the assumption that acetylcholine acts as a synaptic transmitter of the excitatory responses to reticular stimulation in some of the neurons in the sensorimotor cortex. 58 references. (Author abstract modified)

189856 Spehlmann, Rainer; Smathers, Clifford C., Jr. VA Research Hospital, Chicago, IL 60611 **The effects of acetylcholine and of synaptic stimulation on the sensorimotor cortex of cats. II. comparison of the neuronal responses to reticular and other stimuli.** Brain Research (Amsterdam). 74(2):243-253, 1974.

The role of acetylcholine in the synaptic transmission of impulses to the sensorimotor cortex of cats was examined. Stimulation of the nucleus ventralis thalami produced respon-

ses in most neurons. Neurons reacting with short latency response to thalamic stimuli showed a susceptibility to acetylcholine which was similar to that of the other neurons in the pericruciate cortex. Atropine and scopolamine antagonized the effects of extrinsic acetylcholine but they did not block any of the components of the responses to thalamic, transcallosal and pyramidal stimulation: the augmenting response, elicited by repetitive thalamic stimulation, was unaffected. Atropine and scopolamine blocked the excitatory responses to reticular stimulation of some neurons which also were excitable by acetylcholine without blocking their responses to other stimuli. These agents abolished the facilitatory effect of a conditioning stimulus to the reticular formation on a test response to thalamic stimulation in some instances. 23 references. (Author abstract modified)

189893 Ladinsky, Herbert; Consolo, Silvana; Peri, Giuseppe. Istituto di Ricerche Farmacologiche 'Mario Negri', Via Eritrea 62, 20157 Milan, Italy **Effect of oxotremorine and physostigmine on choline levels in mouse whole brain, spleen and cerebellum.** Biochemical Pharmacology (Oxford). 23(7):1187-1193, 1974.

The effect of oxotremorine and physostigmine on acetylcholine and choline levels in mouse whole brain, spleen, cerebellum and plasma was determined by a radiochemical method. Oxotremorine (0.7mg/kg) and physostigmine (0.5mg/kg) increased choline levels in mouse whole brain and cerebellum but their activities differed in spleen, oxotremorine being highly active in increasing choline while physostigmine was ineffective. It is concluded that both oxotremorine and physostigmine act directly through muscarinic receptors in increasing choline levels in cerebellum. The possibility of the existence of muscarinic receptors in the mouse spleen, a tissue probably lacking cholinergic nerves, is considered. It is postulated that oxotremorine first increases tissue choline which then results in increased acetylcholine synthesis. 23 references. (Author abstract modified)

189895 Baxter, James H.; Beaven, Michael A.; Horakova, Zdenka. National Heart and Lung Institute, National Institutes of Health, Bethesda, MD 20014 **Effects of adrenergic agents, theophylline and other drugs on dextran edema and histamine release in rats.** Biochemical Pharmacology (Oxford). 23(7):1211-1217, 1974.

Pretreatment of rats with various catecholamines, theophylline and dibutyryl cyclic AMP decreased their reaction to dextran and reduced the associated release of histamine into the plasma. Protection by the catecholamines was inhibited by the beta blocker, propranolol. Some of these protective drugs owed their effectiveness in large part to the production of hyperglycemia. It appears likely that they also acted directly on the mast cells to prevent the release of histamine and other vasoactive factors, as previously observed in vitro. Phenoxybenzamine, nicotinamide and ethanol also afforded protection not explainable by effects on blood sugar. 22 references. (Author abstract)

190306 Wauquier, Albert; Niemegeers, Carlos J. E.; Lal, Harbans. Department of Pharmacology, Janssen Pharmacuetica, Research Laboratoria, B-2340 Beerse, Belgium **Differential antagonism by naloxone of inhibitory effects of haloperidol and morphine on brain self-stimulation.** Psychopharmacologia (Berlin). 37(4):303-310, 1974.

In order to delineate separate sites underlying the actions of haloperiodol and morphine, the interaction of naloxone with the action of these two drugs was examined in rats. Haloperidol or morphine sulfate injected subcutaneously, completely suppressed bar pressing for brain self-stimulation in rats implanted with electrodes in the lateral hypothalamus. Haloperidol also caused catalepsy and potosis while morphine produced catatonia with exophthalmia. Naloxone in a dose which was ineffective when given alone, differentially reversed the morphine effects but was without any reversing influence on the actions of haloperidol. 16 references. (Author abstract)

190310 Gerlach, J.; Nielsen, M.; Randrup, A. Research Laboratory Department E, Sct. Hans Hospital, DK-4000 Roskilde, Denmark **Effect of desipramine on rat cortex slices incubated with 3H-dopamine.** Psychopharmacologia (Berlin). 37(4):341-349, 1974.

Rat cortex slices were incubated with 3H-dopamine (3H-DA), and the effect of desipramine (DMI) was studied on the accumulation of 3H-DA and 3H-noradrenaline (3H-NA) in the tissue and the concentrations of 3H-DA and 3H-NA in the incubation medium. All the drugs induced a significant decrease of 3H-NA accumulation in the cortical tissue. The 3H-DA retention varied: cocaine and reserpine caused a significant decrease, FLA 63 a marked, significant increase, and DMI a slight, but significant increase. In the incubation medium, 3H-DA significantly increased after DMI, cocaine and reserpine, and remained unchanged after FLA 63. It is suggested that DMI in cortex slices may exert a double mechanism of action on the final step in the noradrenaline biosynthesis: 1) an inhibition of the 3H-DA uptake at the level of the noradrenergic cell membrane; and 2) an inhibition of the intraneuronal transport of 3H-DA to sites where it is converted to 3H-NA, concomitant with an increased intraneuronal 3H-DA accumulation. 25 references. (Author abstract modified)

190311 Janiec, W.; Korczak-Dziuba, K.; Herman, Z. S. Department of Pharmacology, Silesian School of Medicine, 41-200-Sosnowice ul. Jagiellonska 4, Poland **Effect of phenothiazine neuroleptic drugs and tricyclic antidepressants on phosphodiesterase activity in rat cerebral cortex.** Psychopharmacologia (Berlin). 37(4):351-358, 1974.

The activity of phosphodiesterase (PDE) of rat cerebral cortex following the administration in vitro and in vivo of various concentrations of neuroleptic phenothiazine drugs and tricyclic antidepressive drugs was investigated. It has been shown that PDE activity is inhibited by phenothiazine neuroleptic drugs (fluphenazine, trifluperazine, thioproperazine, chlorpromazine and thioridazine in decreasing order, respectively). Tricyclic antidepressants nortiptyline, chlormipramine, protiptyline, imipramine and desipramine caused 60-80% inhibition of PDE activity. It has also been found that the investigated phenothiazine compounds inhibit the high affinity PDE activity more than the PDE activity of low affinity to the substrate. The results obtained suggest that the mechanism of the neuroleptic action of phenothiazine drugs is partially connected with their influence on cyclic 3',5'-adenosine monophosphate metabolism. 28 references. (Author abstract)

190337 Poitou, P.; Guerinot, F.; Bohuon, C. Laboratoire de Biologie Clinique et Experimentale, Institut Gustave-Roussy, F-94800 Villejuif, France **Effect of lithium on central metabolism of 5-hydroxytryptamine.** Psychopharmacologia (Berlin). 38(1):75-80, 1974.

The effect of lithium on central metabolism of 5-hydroxytryptamine was examined. The administration of lithium carbonate for 5 days to rats increased the synthesis rate of brain serotonin, without modifying the brain level of the amine. This increase was not due to a modification of the free tryptophan

in the blood. The level of serotonin and 5-hydroxyindoleacetic acid remained unchanged in seven areas of brain. 22 references. (Author abstract)

190346 Fuller, Ray W.; Snoddy, Harold D.; Slater, Irwin H. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Metabolic interactions between nortriptyline and thioridazine in rats.** Toxicology and Applied Pharmacology. 29(2):259-269, 1974.

The metabolic interactions between nortriptyline and thioridazine in rats were examined. Plasma drug concentrations in rats were higher when nortriptyline was given in combination with thioridazine than when nortriptyline was given alone, regardless of whether the route of administration was po, ip, or iv. Nortriptyline concentrations in brain were also elevated, and the half-life of nortriptyline in brain was prolonged, after thioridazine administration. Although metabolites of thioridazine reacted in the assay for plasma nortriptyline, the elevated drug contents were found to be due to nortriptyline, not to thioridazine metabolites. Hypothermia occurred in rats given large oral doses of thioridazine, but not nortriptyline; greater hypothermic effects were produced by the drug combination. Large ip doses of nortriptyline produced marked hypothermia and gave high plasma drug concentrations comparable to those found when oral nortriptyline was given in combination with thioridazine. 7 references. (Author abstract modified)

190476 Pert, Candace B.; Aposhian, David; Snyder, Solomon H. Dept. of Pharmacology and Experimental Therapeutics, Johns Hopkins Univ. School of Medicine, Baltimore, MD 21205 **Phylogenetic distribution of opiate receptor binding.** Brain Research (Amsterdam). 75(2):356-361, 1974.

The phylogenetic distribution of opiate receptor binding in some vertebrates and some invertebrate nervous tissue is reported. Regional variations in opiate receptor binding is reported for monkeys, humans, rats, chicks, goldfish, dogfish, mice, toads, turtles, crabs, crayfish, snails, squids, mosquitoes, cockroaches and tarantulas. The chemical specificity of the opiate receptor appeared to be the same among a wide range of vertebrates. The failure of the receptor to undergo marked changes throughout evolution may indicate that its confirmation has been severely constrained by the requirement for a good steric fit with an endogenous ligand which is the same for all vertebrates. The inability to demonstrate stereospecific opiate receptor binding in invertebrates suggests that these drugs are incapable of eliciting specific pharmacological responses in invertebrates. 18 references.

190545 Miller, Richard; Horn, Alan; Iversen, Leslie; Pinder, Roger. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge, CB2 2QD, England **Effects of dopamine-like drugs on rat striatal adenyl cyclase have implications for CNS dopamine receptor topography.** Nature (London). 250(5463):238-241, 1974.

The dopamine sensitive adenyl cyclase of the rat striatum was studied in order to define some of the structural requirements for dopamine receptor agonists. Addition of low concentrations of dopamine to rat striatal homogenates increased cyclic-AMP accumulation during a brief incubation in vitro. Dopamine and its N-methyl derivative epinine had similar activities as agonists. Results may be important in the design of future dopamine receptor stimulating agents. In particular, rigid analogs of dopamine such as 2-amino-6,7-dihydroxy-1,2,3,4-tetrahydronaphthalene or other similar compounds may be useful anti-Parkinsonian drugs. 26 references.

190718 Matin, S. B.; Callery, P. S.; Zweig, J. S.; O'Brien, A.; Rapoport, R.; Castagnoli, N., Jr. School of Pharmacy, University of California, San Francisco, CA 94143 **Stereochemical aspects and metabolite formation in the in vivo metabolism of the psychotomimetic amine, 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane.** Journal of Medicinal Chemistry. 17(8):877-882, 1974.

The fate of the psychotomimetic amine 1-(2,5-dimethyoxy-4-methylphenyl)-2-aminopropane (compound 1) was investigated in rabbits. Compound 1 was resolved via its o-nitrotartranilate salts and the absolute configurations were (S)-(+) and (R)-(-). Determination of the enantiomeric composition of unmetabolized amine excreted in the urine of rabbits treated with racemic 1 established the R/S ratio to be equal to or greater than 1. With the aid of 1-14C (labeled at the benzylic position) it was established that 1 was extensively metabolized by the rabbit, and of several suspected metabolites only 1-(2,5-dimethoxy-4-carboxyphenyl)-2-aminopropane was excreted to any great extent. 26 references. (Author abstract modified)

190727 Barker, J. L.; Nicoll, R. A.; Padjen, A. National Institute of Child Health and Human Development, Bethesda, MD 20014 **Studies on convulsants in the isolated frog spinal cord. I. antagonism of amino acid responses. (Unpublished paper)** Washington, D.C., NIMH, 1974, 28 p.

The isolated frog spinal cord was used to study the effects of picrotoxin, bicuculline, and strychnine on the responses of primary afferents to amino acids. A series of neutral amino acids was found to depolarize primary afferents and optimal activity was obtained by an amino acid whose carboxyl and amino groups were separated by a three carbon chain length (GABA). Amino acids with shorter or longer distances between the charged groups were less potent and imidazoleacetic acid was the most potent depolarizing agent tested. Picrotoxin and bicuculline antagonized the primary afferent depolarizations of a number of amino acids with equal specificity. Depolarizing responses to standard concentrations of beta-alanine and taurine were completely blocked by these convulsants while depolarizations to GABA were only partially antagonized. Glycine responses were unaffected by these agents. Strychnine completely blocked beta-alanine and taurine depolarizations and incompletely antagonized several other neutral amino acids. GABA, glutamate and glycine depolarizations were not affected. 42 references. (Author abstract modified)

190829 Segal, Menahem. Laboratory of Neuropharmacology, Special Mental Health Research Division IRP, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Lithium and the monoamine neurotransmitters in the rat hippocampus.** Nature (London). 250(5461):71-73, 1974.

An attempt to elucidate a possible mode of action of lithium (Li) in the rat hippocampus is described. This was done by searching for possible interactions between the effects of iontophoretically applied lithium and several putative neurotransmitters, as well as the electrical stimulation of the locus coaruleus on firing rates of hippocampal pyramidal cells. The data are compatible with the view that Li+ could block the noradrenaline receptor through an action on cyclic AMP synthesis, although earlier alternative assumptions of Li+ action, based on such findings as increased uptake of noradrenaline by brain synaptosomes decrease in the release of noradrenaline and serotonin from brain slices, cannot be eliminated. The iontophoretic mode of application, in spite of its many advantages, test the acute effects of a chronic Li+ treatment. Further electrophysiological study of Li+ actions in

a chronically treated preparation are required to clarify these possibilities. 12 references.

190907 Wagner, Lorin A.; Koerker, Robert L.; Schneider, F. H. Dept. of Pharmacology, University of Pittsburgh, School of Pharmacy, Pittsburgh, PA **Influence of different anions on tyramine and amphetamine uptake by cow adrenal medulla chromaffin vesicles.** Journal of Phamarcy and Pharmacology (London). 26(6):464-467, 1974.

The uptake of (3H)tyramine hydrochlorine and (3H)amphetamine sulphate was measured in a cow adrenal medulla chromaffin vesicle fraction suspended in an incubation medium. It is concluded that the uptake and retention of tyramine by isolated chromaffin vesicles of the cow adrenal medulla is much greater than uptake and retention of amphetamine and that apparent binding of (3H)tyramine is probably not due to binding of a metabolite since inhibition of monoamine oxidase, which is capable of oxidative deamination of tyramine, did not decrease the uptake; and that uptake of tyramine is reduced at low temperature, whereas the uptake of amphetamine is generally unaffected by temperature. It is noted that, of the media studied, uptake of both amines was greatest in an incubation medium of sodium sulphate. 4 references.

191057 Vore, Mary; Sweetman, Brian J.; Bush, Milton T. Dept. of Pharmacology and Toxicology, School of Medicine, Univ. of California, San Francisco, CA 94143 **The metabolism of 1-n-butyl-5,5-diethylbarbituric acid (N-n-butyl barbital) in the rat.** Journal of Pharmacology and Experimental Therapeutics. 190(2):384-394, 1974.

The metabolism of N-n-butyl barbital (nBB) in the rat was determined using the carbon 14 and 14C, 15N labeled compound. The metabolites formed in vivo and by the post-mitochondrial fraction of liver were characterized and identified by gas chromatography - mass spectrometry, countercurrent distribution, partition coefficients, pK and Rf values. Rats given 14C nBB excreted 70 to 90% of the 14C in the urine and 19% to 7% in the feces. Of the 14C excreted in the urine, 70% was identified as a conjugate of N-(3-hydroxy-n-butyl)-barbital(31-OH-nBB), 13% as N-(2,3-dihydroxy-n-butyl)-barbital and 3% as 3'-OH-nBB. When 14C, 15N-nBB was incubated with the 900 times g supernatant from liver, 80% of the total metabolite formed after 60 min was identified as 3'-OH-nBB, 6% as N-(3-keto-n-butyl)-barbital and 4% as N-(2-hydroxy-n-butyl)-barbital (2'-OH-nBB). Pretreatment of rats with phenobarbital for 4 days caused a fivefold increase in the rate of metabolism and drastically altered the ratio of 3'OH-nBB to 2'-OH-nBB. Thus after 60 min incubation, 47% of the total metabolite formed was identified as 3'-OH-nBB and 30% as 2'-OH-nBB. 27 references. (Author abstract)

191121 Titova, V. G.; Korolenko, T. A. Novosibirsk Medical Institute, Novosibirsk, USSR **/The effect of chlorpromazine and stelazine on lysosomes of rat liver during acute intoxication./** Vliyaniye aminazina i stelazina na lizosomy pecheni krys pri ostroy intoksikatsii. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(8):77-79, 1973.

The effect of chlorpromazine and stelazine on the lysosomes of rat livers during acute intoxication was studied. The level of free activity of the marker enzymes indicated the condition of the lysosome membranes. Chlorpromazine (30mg/kg) produced a labile action, that is, increased the free action of acid phosphatase, which indicated that the membrane had been injured. Stelazine did not produce a similar effect because of the smaller dosage (4mg/kg) and probably because it reacts differently with the membrane. 11 references.

191122 Absava, G. I. Institute of Pharmacology of the USSR Academy of Sciences, Moscow **/The influence of psychostimulants on K42 membrane permeability in various portions of rat brain./** Vliyaniye psikhostimulyatorov na membrannuyu pronitsayemost' dlya K42 v raznykh otdelakh golovnogo mozga krys. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(8):81-83, 1973.

The effect of psychostimulants on the incorporation of K42 into the tissues of various portions of the rat brain was studied. Phenamine (2.5mg/kg) and pyridrol (12.5mg/kg) diminished the permeability of the diencephalon and mesencephalon for K42. The effect was absent in the cortex of the great hemispheres. Caffeine (25mg/kg) increased the incorporation of the isotope into the tissue of the cerebral hemispheres but did not affect permeability of the diencephalon and mesencephalon. Phenamine and caffeine elevated, and pyridrol failed to influence the permeability of the medulla oblongata. 17 references. (Author abstract modified)

191281 MacFarlane, M. David; Besbris, Howard. 233 South Beverly Dr., Suite 100, Beverly Hills, CA 90212 **Procaine (Gerovital H3) therapy: mechanism of inhibition of monoamine oxidase.** Journal of the American Geriatrics Society. 22(8):365-371, 1974.

The mechanism by which Gerovital H3 (GH3), a specially stabilized form of procaine hydrochloride, produces a weak inhibition of the enzyme, monoamine oxidase (MAO), was studied by several methods. Purified rat brain mitochondrial MAO was used as the enzyme source and the reaction velocities were determined by quantitating the rate of appearance of 4-hydroxquinoline from kynuramine. Data on dilutional studies with preincubated enzyme inhibitor complexes, as well as other data, strongly indicate that GH3 was a reversible inhibitor of MAO. Analysis of Lineweaver-Burk and Dixon plots obtained by determining the velocity of oxidation of kynuramine with various concentrations of substrate and inhibitor, shows that GH3 is a fully competitive inhibitor of MAO. The weak, reversible, fully competitive inhibition of MAO produced by GH3 is in marked contrast to the potent, irreversible inhibition of MAO produced by currently available agents. The mechanism by which GH3 inhibits MAO may help explain the absence of severe adverse reactions with GH3 that are traditionally associated with irreversible MAO inhibitors in the treatment of depressive illness. 28 references. (Author abstract modified)

191300 Achee, F. M.; Togulga, G.; Gabay, S. VA Hospital, Brockton, MA 02401 **Studies of monoamine oxidases: properties of the enzyme in bovine and rabbit brain mitochondria.** Journal of Neurochemistry (Oxford). 22(5):651-661, 1974.

The enzymatic properties of monoamine oxidase of brain mitochondria were studied in rabbit and bovine cerebral cortex. Five substrates were used for characterization of the enzyme: dopamine, kynuramine, serotonin, tryptamine and tyramine. It was found that there was considerable substrate variation in the properties, but in general, the two species showed similar characteristics. Substrate specificity from Vmax values in decreasing order was tyramine, dopamine, kynuramine, serotonin and tryptamine for the bovine enzyme and tyramine, kynuramine, dopamine, serotonin and tryptamine for rabbit. The activity with tyramine was highly sensitive to increased oxygen tension while kynuramine showed no sensitivity. It is proposed that the properties of monoamine oxidase, a membrane bound enzyme, might be influenced by the microenvironment and results are also discussed in terms of multiple forms or multiple activity sites on a single form. 59 references. (Author abstract modified)

191313 Miller, Carol A.; Levine, E. M. Department of Anatomy, Albert Einstein College of Medicine, Bronx, NY 10461 **Effects of aluminum salts on cultured neuroblastoma cells.** Journal of Neurochemistry (Oxford). 22(5):751-758, 1974.

Neuroblastoma cells, capable of morphologic and biochemical differentiation in monolayer culture, were exposed to medium containing aluminum phosphate. Such treatment resulted in an abundant accumulation of 100 angstrom neurofilaments after 6 days of continuous exposure to the aluminum salt. While growth rates and incorporation of radioactive thymidine in treated cells remained similar to controls, total cellular protein, and incorporation of radioactive leucine were significantly increased. Paradoxically, when the protein content of aluminum treated cultures was maximal these cultures contained about 20% less ribosomal RNA per cell than control cultures. Activity of an important neuronal protein, i.e. acetylcholinesterase, was depressed in treated cultures to a level below control values. 39 references. (Author abstract modified)

191315 Doherty, J. D.; Matsumura, F. Department of Entomology, University of Wisconsin, Madison, WI 53706 **DDT effect on 32P incorporation from gamma-labelled ATP into proteins from lobster nerve.** Journal of Neurochemistry (Oxford). 22(5):765-772, 1974.

The effect of the insecticide DDT (Dichlorodiphenyltrichloroethane) on the amount of 32P from adenosine triphosphate (ATP) incorporated into proteins derived from lobster peripheral nerves was studied. When a high concentration of ATP was used, DDT inhibited the incorporation and reversed the increased incorporation caused by ouabain. At low concentration of ATP, DDT inhibited the incorporation of 32P when the buffer contained magnesium and sodium or potassium alone, but when the buffer contained magnesium and both sodium and potassium together, DDT consistently caused an increased amount of 32P to be incorporated. The proteins that were affected by DDT were microsomal in nature and could be centrifuged from supernatant by recentrifuging at 149,000 g. The possibility that this system may be the actual target through which DDT causes its characteristic interferences of the ionic conductance changes associated with the action potential is discussed. 17 references. (Author abstract modified)

191319 Storm-Mathisen, J.; Guldberg, H. C. Norwegian Defence Research Establishment, Division for Toxicology, PO Box 25-N-2007, Kjeller, Norway **5-Hydroxytryptamine and noradrenaline in the hippocampal region: effect of transection of afferent pathways on endogenous levels, high affinity uptake and some transmitter-related enzymes.** Journal of Neurochemistry (Oxford). 22(5):793-803, 1974.

The effect of transection of afferent pathways on endogenous levels, high affinity uptake and some transmitter related enzymes of 5-hydroxytryptamine (5-HT) and noradrenaline (NA) were examined in the hippocampal region of the rat brain. The dorsal route, consisting of fimbria, fornix superior and cingulum, was estimated to supply about 75% of the 5-HT fibers and 40% of the containing fibers. The ventral route, allegedly passing through the amygdaloid area, accounts for the rest. The cingulum bundle contributes a definite part of the 5-HT fibers but very few of the NA fibers. No evidence was found for an intrinsic origin of monoaminergic fibers in the hippocampal region. Monoamine oxidase and catechol-O-methyltransferase showed no change following the lesions and are considered to be localized predominantly outside the aminergic neurons. The results on DOPA decarboxylase indicate that about 50% of the enzyme is situated outside 5-HT and NA nerves. 67 references. (Author abstract modified)

191324 Haschke, R. H.; Byers, Margaret R.; Fink, B. Raymond. Department of Anesthesiology, University of Washington, Seattle, WA 98195 **Effects of lidocaine on rabbit brain microtubular protein.** Journal of Neurochemistry (Oxford). 22(5):837-843, 1974.

The effects of lidocaine on rabbit brain microtubular protein were examined. Microtubule repolymerization from a crude supernatant fraction prepared from rabbit brain was followed quantitatively by viscometry and electron microscopy. Lidocaine inhibits this repolymerization in a dose dependent fashion and the effect is completely reversible upon removal of the lidocaine by dialysis. Direct counting of microtubules by electron microscopy indicates that the local anesthetic dereases the number of tubules without significantly affecting their length. Procaine and etidocaine were also found to affect the polymerization of microtubules with results similar to those found with lidocaine. 8 references. (Author abstract modified)

191326 Juorio, A. V.; Gabella, G. Psychiatric Research Unit, University Hospital, Saskatoon, Saskatechewan S7N 0W8, Canada **Noradrenaline in the guinea pig alimentary canal: regional distribution and sensitivity to denervation and reserpine.** Journal of Neurochemistry (Oxford). 22(5):851-858, 1974.

The concentrations of noradrenaline, dopamine and 5-hydroxytryptamine were studied in the stomach, duodenum, ileum, caecum (taenia coli), colon and rectum of the guinea pig. In the longitudinal muscle - myenteric plexus, the amount of noradrenaline was lower in the ileum, higher in the duodenum and caecum, and even higher in the stomach and rectum. The highest value was found in the colon, probably related to the occurrence of intramural adrenergic neurons. When extrinsic nerves to the ileum were damaged, the amount of noradrenaline in the corresponding ileal segment was reduced to less than 5% within 3 days in both fractions of the wall. 6-Hydroxydopamine reduced to 33% the amount of noradrenaline in longitudinal muscle - myenteric plexus of ileum and colon. Reserpine reduced the amount of noradrenaline in the longitudinal muscle - myenteric plexus of both ileum and colon. Doses of reserpine as small as 0.02mg/kg were still effective in causing a great reduction in noradrenaline concentration. No difference in the effects on ileum and colon was observed. 41 references. (Author abstract modified)

191331 Urquhart, Nadine; Perry, T. L.; Hansen, Shirley; Kennedy, Janet. Department of Pharmacology, University of British Columbia, Vancouver 8, British Columbia, Canada **Passage of taurine into adult mammalian brain.** Journal of Neurochemistry (Oxford). 22(5):871-872, 1974.

The passage of labeled taurine into the adult mammalian brain was examined in adult rats and monkeys. Taurine was administered orally to the rats and i.p. to the monkeys. After a correction made for the radioactivity which accounted for blood trapped in the brains a substantial amount of labeled taurine was found in the rat and monkey brains. Radioactivity in taurine accounted for 99.3% of the total radioactivity in the whole brain of the rat and 98.7% of the total activity in the cerebral cortex of the monkey. Administration of 0.25mmol/kg of taurine to fasting human adults raised the concentrations of taurine in plasma. It is concluded that the oral administration of taurine might prove effective in correcting a taurine deficiency in human brain. 6 references.

191380 Phillis, John W. Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Canada **Neomycin and ruthenium red antagonism of monoaminergic depression of cerebral cortical neurones.** Life Sciences (Oxford). 15(2):213-222, 1974.

Neomycin and ruthenium red, two agents which are known to interfere with the transport and binding of calcium, were found to antagonize the depressant actions of noradrenaline and 5-hydroxytryptamine on cerebral cortical neurons in rats. Ouabain and sodium azide, metabolic inhibitors, also block the action of noradrenaline. These findings support suggestions that monoaminergic depression of cortical neurons involves a calcium dependent mechanism which may be linked to a membrane ion pump. 21 references. (Author abstract)

191383 Tonge, Sally R. School of Pharmacy, Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, England **Permanent alterations in 5-hydroxytryptamine metabolism in discrete areas of rat brain following exposure to drugs during the period of development.** Life Sciences (Oxford). 15(2):245-249, 1974.

5-Hydroxytryptamine metabolism was examined in rats administered methylamphetamine, chlorpromazine, phencyclidine and imipramine. during pregnancy and the suckling period. Male offspring were given no drugs after weaning until 9 months later; groups were then injected with p-chlorophenylalanine or saline, killed 9 hours later and the brains dissected into eight areas. Exposure to methylamphetamine, chlorpromazine or phencyclidine during the period of brain development was found to have had permanent effects both on 5-hydroxytryptamine concentrations and on the rate of depletion after synthesis blockade. 13 references. (Author abstract)

191389 Hartse, K. M.; Rechtschaffen, A. Sleep Laboratory, University of Chicago, 5741 South Drexel Avenue, Chicago, IL 60637 **Effect of atropine sulfate on the sleep-related EEG spike activity of the tortoise, Geochelone carbonaria.** Brain, Behavior and Evolution (Basel). 9(2):81-94, 1974.

To evaluate the correspondence between mammalian slow wave sleep (SWS) and reptilian spikes, atropine sulfate, a centrally acting cholinergic blocking agent which increases slow waves in mammals, was administered to ten tortoises, Geochelone carbonaria, chronically implanted for electroencephalogram and electrocardiogram recordings. A dramatic increase in spike activity was seen within 4-12 h after atropine sulfate administration relative to saline injection. By hours 37-48 postinjection there was no significant statistical difference in spike rates between saline and atropine sulfate conditions. Atropine methyl nitrate had no statistically significant effect upon spike rates for the first 12 h postinjection. Baseline rates of spiking and spike rates after saline injection were not significantly different. These results support the analogy of mammalian SWS and reptilian spikes. Both are increased after administration of atropine sulfate, and both are centrally mediated phenomena. 25 references. (Author abstract modified)

191411 Von Schwartzenfeld, I.; Bures, J. Institut fur Pharmackologie und Toxikologie der Medizinischen Akademie Carl Gustav Carus, 801 Dresden, Lingnerplatz 1, Germany **The effect of cholinomimetic drugs on potassium transport in rat cerebral cortex.** BRain Research (Amsterdam). 77(1):77-84, 1974.

Potassium selective microelectrodes were used in rats to test the hypothesis that the cholinomimetic effect of arecoline is mediated by changes of potassium transport. Arecoline did not influence the resting level of extracellular potassium (K+) in the cerebral cortex of unanesthetized curarized rats, but reduced by 43% the rate of K+ removal from an epidural KC pool. This latter effect was markedly enhanced when 50mM KC with o.1mM ouabain were used in the pool. Scopolamine did not change the rat of K+ removal but prevented the arecoline effect when applied 5 min before arecoline administration. Arecoline slightly increased extracellular K+ in the surface layers of cerebral cortex below the pool. It is concluded that arecoline and ouabin induced slowing of K+ removal is due to interference with K+ transport across the cerebral tissue into blood capillaries. 33 references. (Author abstract)

191413 Teller, David N.; De Guzman, Teresita; Lajtha, Abel. New York State Research Institute for Neurochemistry and Drug Addiction, Ward's Island, New York, NY 10035 **The mode of morphine uptake into brain slices.** Brain Research (Amsterdam). 77(1):121-136, 1974.

The uptake of (N-14C methyl)morphine into rat, mouse, or guinea pig brain slices was studied. Methods are described for the extraction and thin layer chromatography of morphine at 96% recovery levels, and for the determination of 14C at 70-90% counting efficiency with brain tissue samples are described. After morphine had been in the tissue for 30 min, 96% of the radioactivity was extractable, and 99% of this was unmetabolized morphine. Strong metabolic inhibitors, e.g. cyanide, at concentrations that completely block amino acid transport, did not markedly reduce the uptake of morphine. The uptake into and efflux from brain tissue was not affected by concentrated morphine, analogs, or narcotic antagonists. The uptake of morphine showed no signs of the competitive inhibition that is typical of active transport processes. Morphine uptake was not affected by acute or chronic morphine injections in the mouse or guinea pig. The uptake of morphine into brain tissue was also temperature dependent, but it occurred at 0.5degrees C and also after the tissue was kept at 95 degrees C for 10 min. 25 references. (Author abstract modified)

191418 Burki, Hans R.; Ruch, Walter; Asper, Helmuth; Baggiolini, Marco; Stille, Gunther. Research Institute Wander, Sandoz Research Unit, Berne, Switzerland **Effect of single and repeated administration of clozapine on the metabolism of dopamine and noradrenaline in the brain of the rat.** European Journal of Pharmacology (Amsterdam). 27(2):180-190, 1974.

The action of clozapine on the synthesis and disappearance of catecholamines in the rat brain was compared with that of four typical (i.e. cataleptogenic) neuroleptics, haloperidol, chlorpromazine, loxapine, and the 2-chloro isomer of clozapine, HF-2046. Clozapine enhances the dopamine content of the striatum while the typical neuroleptics always decrease the dopamine level, probably as a consequence of turnover stimulation. Upon repeated administration, the dopamine enhancing effect of clozapine becomes more pronounced while the dopamine turnover stimulation caused by typical neuroleptics diminishes. At high doses, clozapine also stimulates disappearance of dopamine as shown by the accumlation of homovanillic acid. Clozapine stimulates the turnover of NA in the brain stem of the rat, but this effect is markedly diminished upon repeated administration. It appears that clozapine acts on the NA system of brain stem in a way similar to that of the typical neuroleptics. 39 references. (Author abstract modified)

191420 Offermeier, Johan; Van Den Brink, Frans G. Department of Pharmacology, University of Potchefstroom, Potschefstroom, South Africa **The antagonism between cholinomimetic agonists and beta-adrenoceptor stimulants: the differentiation between between functional and metaffinoid antagonism.** European Journal of Pharmacology (Amsterdam). 27(2):206-213, 1974.

The antagonism between cholinomimetic agonists and beta-adrenoceptor stimulants was examined in smooth muscle of calf and guinea pig tracheal muscle. The shifting of a methacholine curve by atropine or pentyltriethylammonium was compared with the shifts caused by l-isoprenaline and by combinations of atropine or pentyltriethylammonium and l-isoprenaline. The influence of the absence of a reserve in the cholinergic system (realised by preincubation with phenoxybenzamine or by using the partial cholinomimetic agonist proploxapropanium) on sets of curves of a beta-adrenoceptor stimulant made in the presence of a cholinomimetic agonist, and vice versa, was determined. Since in each experiment the results agree with the expectations based on the current model of functional interaction but cannot be explained with the metaffinoid model, the classification of the antagonism in question as functional antagonism seems justified. 17 references. (Author abstract modified)

191421 Ahtee, Liisa. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Catalepsy and stereotypies in rats treated with methadone; relation to striatal dopamine.** European Journal of Pharmacology (Amsterdam). 27(2):221-230, 1974.

To study methadone induced catalepsy and stereotyped behavior, rats were treated for 8 weeks with methadone. Acute administration of 10mg/kg of methadone produced catalepsy but no stereotypies in control rats. After 5 weeks of chronic administration methadone still produced dose dependent catalepsy, the degree of which gradually decreased with continuing treatment. Naloxone administered before methadone completely prevented the appearance of catalepsy and stereotypy. Two hours after methadone, the striatal homovanillic acid (HVA) concentration of rats receiving methadone for 8 weeks was increased to about the same degree as in control (saline) rats receiving the same dose of methadone as a single injection. The results suggest that the primary effect of methadone is catalepsy which causes increased dopamine production as a compensatory mechanism. The additional dopamine is a probable cause of stereotyped behavior in rats which are partially tolerant to the cataleptic effect of methadone. 35 references. (Author abstract modified)

191422 Jori, Armanda; Cecchetti, Giancarlo; Dolfini, Monti, Elenaj Enzo; Garattini, Silvio. Istituto di Ricerche Farmacologie Mario Negri, Via Eritera 62, 20157 Milan, Italy **Effect of piribedil and one of its metbolites on the concentration of homovanillic acid in the rat brain.** European Journal of Pharmacology (Amsterdam). 27(2):245-248, 1974.

The effect of piribedil and one of its metabolites on the concentration of homovanillic acid (HVA) in the rat brain was examined. Piribedil and its metabolite (pyrimidyl-2')-1(dihydroxy-3',4'-benzyl)-4-piperazine dichlorphydrate (PdHBP), like apomorphine, decrease the level of HVA in the rat striatum. The effect appears rapidly and it lasts for about 2 hr. Piribedil antagonizes the rise of striatal HVA elicited by chlorpromazine, haloperidol and fenfluramine. Pirbedil, PdHBP and apomorphine did not counteract the increase of striatal HVA induced by d-amphetamine. 25 references. (Author abstract)

191423 Consolo, Silvana; Ladinsky, Herbert; Peri, Giuseppe; Garattini, Silvio. Istituto di Ricerche Farmacologiche Mario Negri, Via Eritrea 62, 21057 Milan, Italy **Effect of diazepam on mouse whole brain and brain area acetylcholine and choline levels.** European Journal of Pharmacology (Amsterdam). 27(2):266-268, 1974.

The effect of diazepam on mouse whole brain and brain area acetylcholine and choline levels was studied. A single i.v. dose of diazepam increased mouse whole brain acetylcholine levels. Choline levels, choline acetyltransferase and acetylcholinesterase activities were not affected, which is consistent with the hypothesis that diazepam blocks release of acetylcholine. Diazepam increased acetylcholine levels in the hemispheres and diencephalon but not in the cerebellum or mesencephalon. The effect lasted for 4 hr in the hemispheres and for 30 min in the diencephalon. This short lasting biochemical action precludes a correlation with the long lasting action of diazepam against pentylenetetrazole. 14 references. (Author abstract)

191495 Roizen, Michael F.; Moss, Jonathan; Kopin, Irwin. Department of Anesthesia, University of California San Francisco Medical Center, San Francisco, CA **Effect of anesthetic agents on peripheral sympathetic nervous system function as monitored by arterial plasma catecholamine levels. (Unpublished paper)** Bethesda, MD, NIMH, 1974. 10 p.

The effect of several anesthetics on total plasma catecholamines and norepinephrine was studied by radioisotopic enzymic techniques in Sprague-Dawley rats. A striking decrease in levels of both total plasma catecholamines and norepinephrine was found in rats anesthestized with halothane, cyclopropane, pentobarbital, ketamine hydrochloride, urethane or chloralose. Changes in arterial catecholamines did not wholly parallel changes in blood pressure. Results suggest that the cardiovascular effects of the anesthetics cannot be solely attributed to their sympathoadrenal effects. 21 references.

191496 Sandler, Merton; Youdim, Moussa B. H.; Pare, Charles M. Queen Charlotte's Maternity Hospital, London, England **Multiple forms of MAO: some in vivo correlations.** Psychopharmacology Bulletin. 10(3):5-6, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, evidence from in vivo observations was presented which suggests that more than one type of monoamine oxidase (MAO) activity is likely to function within the cell. Results of a study on rats were inconclusive, but a significant deficit of phenylethylamine and tyramine oxidizing ability was noted in platelet samples from migrainous as compared with normal humans. This suggests that a relative decrease of MAO B is important in the pathogenesis of migraine, but the manner in which these data relate to an earlier observed sulfate conjugation deficit for tyramine in one variety of migraine remains to be determined. Preliminary evidence has also been obtained that decreased conjugating ability (or, perhaps, increased MAO activity) is a further physical concomitant of depressive illness, the effect being reversed when the patient returns to normal.

191497 Youdim, Moussa B. H.; Holzbauer, M.; Woods, H. F. MRC Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford, England **Physico-chemical properties, development, and regulation of central and peripheral monoamine oxidase activity.** Psychopharmacology Bulletin. 10(3):6-7, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, some of the factors which control monomine oxidase (MAO) activity were reported. Results of the investigation indicate that the properties of MAO may differ depending on the type of preparation studied. The substrate inhibition of liver MAO with kynuramine as substrate, which occurs when purified enzyme preparations are used, does not occur in isolated perfused liver, although the kynuramine concentration giving half maximal rates of reaction in the organ is close to Km found using the pure enzyme. Findings partially support the concept that the preservation of the structural integrity of an organ at the gross and microscopic level, together with such features as permeability barriers, are of great importance in the control of MAO activity and must be taken into consideration if conclusions regarding the control of monoamine metabolism are to be drawn from results obtained using experimental models. 14 references.

191503 Lewander, Tommy. Psychiatric Research Center, University of Uppsala, Ulleraker Hospital, Uppsala, Sweden **Effect of chronic treatment with central stimulants on brain monoamines and some behavioural and physiological functions in rats, guinea pigs, and rabbits.** Psychopharmacology Bulletin. 10(3):11-12, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the effect of chronic treatment with central stimulants on brain monoamines in rats, guinea pigs, and rabbits was discussed, along with some behavioral and physiological functions of these drugs in the animals. Brain noradrenaline (NA), dopamine (DA), homovanillic acid (HVA), tryptophan, serotonin (5-hydroxytryptamine, 5-HT), and 5-hydroxyindole acetic acid (5-HIAA) were measured fluorometrically after acute or chronic dl-amphetamine (AM) treatment. In rat brains, NA decreased to 40%-60% of the controls after acute or chronic AM treatment in doses of 16-32mg/kg i.p. Similar results occurred in guinea pigs and rabbits where species formation and accumulation of p-hydroxynorephedrine, a metabolite of AM, into central and peripheral NA neurons does not take place. The development and disappearance of tolerance to the hyperthermic effect of d-AM was related to brain AM concentrations and to changes in brain NA, DA, tryptophan, and 5-HT levels. Phenmetrazine (Preludin) caused no change in brain NA, DA, 5-HT, or 5-HIAA levels after a single 40-120mg/kg injection. Tolerance to the anorexigenic actions of d-AM, l-AM and phenmetrazine developed to a maximal degree during approximately 10 days of chronic treatment. 7 references.

191509 Molinoff, Perry B.; Nelson, David L.; Orcutt, James C. Department of Pharmacology, University of Colorado Medical Center, Denver, CO **Dopamine-beta-hydroxylase and the regulation of the noradrenergic neuron.** Psychopharmacology Bulletin. 10(3):24-25, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the role of the enzyme dopamine-beta-hydroxylase (DBH) in the regulation of the noradrenergic neuron was discussed. The amount of DBH present in adrenergic nerves appears regulated by the frequency or pattern of impulses in the presynaptic neuron. Administration of drugs which deplete catecholamines and cause hypotension leads to an increase in the activity of DBH. This increase requires nerve impulses and is probably due to an increase in the rate of synthesis of this enzyme. Beta-hydroxylation of dopamine is probably controlled not only by the amount of DBH present in adrenergic nerves, but also by at least two mechanisms which may limit the activity of the enzyme in vivo. The first of these derives from the presence of endogenous inhibitors of DBH which are found in many tissues of the rat and the second involves the unique subcellular localization of DBH. 3 references.

191513 Carlsson, A.; Kehr, W.; Lindquist, M. University of Goteborg, Goteborg, Sweden **Short-term control of tyrosine hydroxylase.** Psychopharmacology Bulletin. 10(3):28, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the short-term control of tyrosine hydroxylase (TH) was discussed. TH can undergo minute to minute adjustments according to need without any change in the total number of enzyme molecules, and an investigation was conducted to determine if end product inhibition is a regulatory mechanism in such activity. Observations argue against such inhibition of TH as a major regulatory mechanism for the adrenal medulla; stimulation of the adrenomedullary nerves caused an increase in dopamine level in the adrenals which occurred in spite of an increased dopamine turnover rate and thus presumably is due to an increased synthesis caused by an activation of the rate limiting TH. By means of the ganglionic blocking agent, chlorisondamine, this effect was dissociated from the release of adrenomedullary hormones. It is concluded that the short-term control of TH occurs mainly by adjusting the availability of an allosteric modulator.

191515 Costa, E.; Guidotti, A.; Zivkovic, B. Laboratory of Preclinical Pharmacology, National Insitute of Mental Health, St. Elizabeths Hospital, Washington, DC **Short- and long-term regulation of tyrosine hydroxylase.** Psychopharmacology Bulletin. 10(3):29-30, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, present understanding of the long-term and short-term regulation of tyrosine hydroxylase (TH) as it transpires from studies conducted in vivo in dopaminergic terminals of the rat striatum and in the chromaffin cells of the adrenal medulla was reported. A form of immediate short-term control of TH is detailed, along with a delayed long-term control of synthesis rate of TH molecules. Research has revealed that neuroleptics increase the pulse flow rate in dopaminergic axons, and it is suggested that the change of the observed affinity constant for TH may be the result of the increased neuronal activity. Accordingly, the long-term increase of TH in medulla was used to study the correlation between the induction of TH and the immediate stimulus coupled increase of the cAMP/cGMP concentration ratio. It is concluded that the stimulus coupled change of cyclic nucleotides in medulla may modify ribosomal function, perhaps by activating ribosomal protein kinase. 5 references.

191516 Mandell, A. J.; Knapp, S. Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA **Regulation of function of tryptophan hydroxylase.** Psychopharmacology Bulletin. 10(3):30-31, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, regulation of the function of tryptophan hydroxylase, the apparent rate limiting enzyme in the biosynthesis of 5-hydroxytryptamine (5-HT), was discussed. The effects of certain drug administrations were reported, demonstrating alterations in synaptosomal capacity to synthes-

ize 5-HT that develop within an hour of drug administration and disappear within a day. Simultaneous comparisons were made between the acute effects of amphetamine on soluble enzyme activity in the lateral midbrain (the origin of most serotonergic input to the striatum), conversion activity in the striatum, and soluble enzyme activity in the striatum. Extending research with the effects of short-term, and long-term administration of lithium carbonate on 5-HT synthesis, a progressive increase in synaptosomal conversion of tryptophan to 5-HT associated with stimulated uptake of substrate in striata from rats that had been treated with lithium carbonate was noted. It is suggested that the complex ongoing regulation of tryptophan hydroxylase activity might involve both changes in the enzyme already available in the nerve ending and changes in enzyme synthesis and transport that may be of short latency and duration. 5 references.

191517 McKenzie, G. M. Department of Pharmacology, Wellcome Research Laboratories, Research Triangle Park, NC **The effects of COMT inhibitors on behavior and dopamine metabolism.** Psychopharmacology Bulletin. 10(3):31-38, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a test was described of the hypothesis that the biochemical changes induced by apormorphine may be the result of catechol-O-methyltransferase (COMT) inhibition. Agroclavine was used, a dopaminergic agonist which is neither a substrate for COMT nor an inhibitor of the enzyme. Results support the contention that the effects of apomorphine on domapine turnover and on chlorpromazine induced changes in turnover may be mediated by an interaction between apmorphine and the enzyme COMT. This is in contrast to the concept that these changes are brought about by the activation of postsynaptic dopaminergic receptors. Findings are consistent, however, with the concept that the behavioral changes following apomorphine are a consequence of postsynaptic dopaminergic receptor activation. 3 references.

191518 Cooper, Barrett R.; Breese, George R. University of North Carolina School of Medicine, Biological Sciences Research Center, Chapel Hill, NC **Relationship of catecholamine neural systems to the behavioral alterations produced by 6-hydroxydopamine administration into brain.** Psychopharmacology Bulletin. 10(3):39, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the acute and chronic behavioral changes produced by intracisternal administration of 6-hydroxydopamine were described. The alterations induced by this compound were related to the destruction of noradrenergic or dopaminergic neural systems in the brain. Results of experimentation with rats treated to reduce brain dopamine indicated that the deficits in animals in which both brain catecholamines were reduced were the result of destroying dopaminergic fibers. Findings support the view that dopaminergic fibers in the brain are responsible for maintenance of a wide variety of behavioral and pharmacological responses. 9 references.

191519 Roth, Robert H.; Walters, Judith R.; Morgenroth, Victor H., III. Department of Pharmacology, Yale University School of Medicine, New Haven, CT **Effects of alterations in impulse flow on transmitter metabolism in central dopaminergic neurons.** Psychopharmacology Bulletin. 10(3):40, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the effects of alterations in impulse flow on transmitter metabolism in central dopaminergic (DA) neurons in vivo and in vitro in rats were reported. Results from in vitro studies suggest that during a cessation of impulse flow, when Ca++ influx and transmitter release are blocked, the lack of available intercellular Ca++ results in an allosteric change in tyrosine hydroxylase, causing a marked increase in tyrosine hydroxylase activity. In vivo administration of DA receptor stimulating agents reverses this increase in activity, possibly by partly restoring Ca++ fluxes and altering the properties of tyrosine hydroxylase in the striatum to a form which is again sensitive to inhibition by endogenous DA.

191526 Breese, George R.; Cooper, Barrett R. Department of Psychiatry, School of Medicine, University of North Carolina, Chapel Hill, NC **Evidence for a dopaminergic involvement in the maintenance of self-stimulation.** Psychopharmacology Bulletin. 10(3):45-46, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, an examination of changes in self-stimulation responding in rats, to test evidence for a dopaminergic involvement in the maintenance of such stimulation was described. Electrodes were implanted in the lateral hypothalamus following 6-hydroxydopamine treatment which depleted brain dopamine, norepinephrine, or both of these catecholamines, and results were reported. Since amphetamine has been proposed to facilitate self-stimulation by indirectly releasing norepinephrine, the possible relationship of the stimulant actions of amphetamine to intact brain catecholamine neural systems was examined in animals in which brain norepinephrine or dopamine was preferentially reduced. In addition, the hypothesis that self-stimulation results from activation of one or both of the catecholamine containing systems was tested and supported. 5 references.

191613 Ebe, Mituru; Homma, Isao; Ishiyama, Yoji. Toranomon Hospital, Tokyo, Japan **Effects of neuroleptic agent on central nervous system of albino rats.** Neurology India (Bombay). 20(Supplement 2):280-283, 1972.

The effects of Droperidol (a neuroleptic agent) on the central nervous system of albino rats were investigated by electroencephalograms ECG) from cortex and hippocampus, visual evoked potential (VEP), electrocardiograms ECG), respiratory rate, and body movement. Both cortical and hippocampal EEGs were stable and unchanged with a small dose, but in larger doses the slow waves and the fast activities increased in amount and in extremely large doses, the EEGs faded out. In small doses, although EEGs apparently were not affected, in the results of the frequency analysis the percentage ratio of the basic rhythm increased in cortical EEG and was stable in hippocampal EEG. The peak latencies in VEP were well correlated with the administered dose, that is, shortened in small dose and delayed in large dose. Pulse rate increased with a small dose and decreased with a large dose; EEG showed no ischemic effects; respiration rate was relatively stable; and the frequency of body movement was reduced depending on the administered dose.

191762 Landis, S. C.; Bloom, F. E. Lab. of Neuropharmacology, NIMH, Wm. A. White Bldg., St. Elizabeths Hospital, Washington, DC 20032 **Fluorescence and electron microscopic analysis of catecholamine-containing fibers in mutant mouse cerebellum. (Unpublished paper).** Washington, D. C., NIMH, 1974. 1 p.

Fluorescence and electron microscopic analysis of catecholamine (CA) containing fibers was reported in mutant

mouse cerebellum. Weanling C57BL and adult outbred staggerer, reeler and weaver mice manifested increased CA fluorescence per unit area in their hypoplastic cerebella than normals. Abundant varicosities were present in each of the three but the patterns of fluorescent fibers were distinctive. Fluorescent fibers appeared more abundant than normal in the cerebellar cortex of adult nervous mice in which 90% of the Purkinje cells had degenerated. Cerebella from the three hypoplastic mutants were fixed with potassium permanganate (KMn04) and examined with the electron microscope. Axonal boutons containing small granular vesicles (SGV) characteristic of CA containing terminals were present, and morphologically similar in all three. Boutons were small or medium in size, had lucent axoplasm and relatively few synaptic vesicles. Incubation of tissue slices in 5-hydroxydopamine (5OHDA) followed by KMn04 fixation caused a four fold increase in the number of boutons containing SGV and an increase in the number of vesicles containing granules in each bouton. Using these techniques to identify CA terminals synapses have been observed on Purkinje dendrites and spines and stellate somata. (Author abstract modified)

191764 Costa, E.; Guidotti, A.; Mao, C. C. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Diazepam, cyclic nucleotides and amino acid neurotransmitters in rat cerebellum. (Unpublished paper).** Washington, D. C., NIMH, 1974. 18 p.

Diazepam, cyclic nucleotides and amino acid neurotransmitters were examined in the rat cerebellum. The data show that diazepam lowers the concentration of cyclic guanosine 3',5'-monophosphate (cGMP) in the cerebellum. Since it fails to act in mice with degenerated Purkinje cells, it was inferred that these cells might be the site of action of diazepam. Selective increase of cGMP could be elicited by harmaline which increased the rate of climbing fiber discharge. The increase was prevented by doses of diazepam which per se failed to decrease cerebellar cGMP. Intraventricular injection of glutamate also increased cGMP in cerebellum. Such an increase could also be antagonized by diazepam. Circumstantial evidence was presented which suggested that gamma-aminobutyric acid and glumatate may exert a reciprocal antagonistic action in regulating cGMP levels and that diazepam may antagonize glutamate. 16 references. (Author abstract modified)

191766 Gerhards, H. J.; Carenzi, A.; Costa, E. Farbwerke Hoechst AG., 6230 Frankfort (M.) 80, West Germany **Effects of nomifensine (HOE 984), d-amphetamine and apomorphine on motor activity, catecholamine turnover and cAMP concentrations in rat brain. (Unpublished paper).** Washington, D. C., NIMH, 1974. 18 p.

An investigation was made of the effects on rats of nomifensine (8-amino-2-methyl-4-phenyl-1,2,3,4-tetrahydroisoquinoline hydrogenmaleate), a new antidepressant with a similar pharmacological profile to the cyclic antidepressants. It was found that: 1) nomifensine increases motor activity, and this increase cannot be blocked by pretreatment with alpha-methyl tyrosine methylester (alpha-MT), but can be blocked by pretreatment with alpha-MT and reserpine in combination; 2) dopamine (DA) and norepinephrine (NE) turnover in striatum and teldiencephalon are not increased by threshold doses of nomifensine which elicit hypermotilitus, but turnover is increased by a dose 10 times the threshold level; 3) nomifensine increases cyclic-AMP concentrations in striatum in a linear dose dependent manner; and 4) nomifensine blocks NE uptake in noradrenergic and DA uptake in dopaminergic neurons very strongly, and it is suggested that this inhibition of DA uptake is responsible for nomifensine's stimulation of motor activity. These findings are compared to the effects observed after similar doses of apomorphine or d-amphetamine. 17 references. (Author abstract modified)

191767 McKearney, James W. Worchester Foundation for Experimental Biology, 222 Maple Ave., Shrewsbury, MA 01545 **Effects of d-amphetamine, morphine and chlorpromazine on responding under fixed-interval schedules of food presentation or electric shock presentation.** Journal of Pharmacology and Experimental Therapeutics. 190(1):141-153, 1974.

Squirrel monkeys responding under fixed-interval (FI) schedules in which behavior was maintained either by food presentation or by presentation of a brief electric shock were given d-amphetamine, morphine, or chlorpromazine. d-Amphetamine increased responding under both the food and shock presentation schedules at intermediate doses and decreased under both schedules at the higher doses. Morphine produced increases in responding under the FI schedules of shock presentation but only decreased responding under the FI schedules of food presentation. Chlorpromazine generally decreased responding under both FI schedules, but decreases in responding were usually proportionately greater under schedules of shock presentation. 39 references. (Author abstract modified)

191768 Falk, John L.; Tang, Maisy; Bryant, Richard W. Dept. of Psychology, Rutgers University, New Brunswick, NJ 08903 **Dipsogenic action of diazoxide: a pharmacologic analysis.** Journal of Pharmacology and Experimental Therapeutics. 190(1):154-164, 1974.

Diazoxide produced a pronounced, dose related, acute, dipsogenic response in water satiated rats. Further studies showed that this dipsogenic action was not secondary to a diuresis or acute changes in blood volume or ionic concentrations. Dose related hypotension was observed. Alpha-adrenergic blocking with tolazoline increased the dipsogenic response to diazoxide by 38%, while the beta-antagonist propranolol decreased the response (by 71% at the largest dose) as a function of dose level. This graded decrease in the dipsogenic response to diazoxide was attributed to an antagonism of its beta-adrenergic action by propranolol, although at the largest dose of propranolol employed, a smaller decrease in the dipsogenic responses induced by water deprivation (16%) and by sodium chloride (35%) was also observed. It was concluded that the drinking response had its origin in a renal beta-adrenergic response, but that the crucial participation of the renin angiotensin system has not been demonstrated. 39 references. (Author abstract modified)

191769 Bhargava, Hemndra N.; Way, E. Leong. Dept. of Pharmacology, School of Medicine, U. of California, San Francisco, CA 94143 **Effect of l-phenyl-3-(2-thiazolyl)-2-thiourea, a dopamine beta-hydroxylase inhibitor, on morphine analgesia, tolerance and physical dependence.** Journal of Pharmacology and Experimental Therapeutics. 190(1):165-175, 1974.

The administration of the dopamine-beta-hydroxylase inhibitor l-phenyl-3-(2-thiazolyl)-2-thiourea (PTT) partially inhibited the development of tolerance to and physical dependence on morphine in the mouse as evidenced by the decrease in the amount of morphine necessary to produce analgesia and the reduction in dependence by the increase in the amount of naloxone necessary to induce precipitated withdrawal jumping after morphine pellet implantation for three days. Further evidence was indicated by a reduction in bodyweight loss

which occurs after abrupt withdrawal from dependent animals. PTT potentiated morphine analgesia but the effect could not be correlated with changes in brain levels or norepinephrine, dopamine, copper, serotonin, acetylcholine, and choline nor with altered brain uptake of morphine. However, there was a decrease in brain serotonin turnover. The inhibition of PTT of naloxone precipitated withdrawal jumping in dependent mice was accompained by an elevation in brain acetylcholine and an inhibition of the sudden rise in dopamine that occurs during precipitated withdrawal. 41 references. (Author abstract modified)

191771 Ordonez, L. A.; Arbrus, M.; Boyson, S.; Goodman, M. N.; Ruderman, N. B.; Wurtman, R. J. Dept. of Nutrition and Food Science, Mass. Instit. of Technology, Cambridge, MA 02139 **Skeletal muscle: reservoir for exogenous L-dopa.** Journal of Pharmacology and Experimental Therapeutics. 190(1):187-191, 1974.

Concentrations of exogenous L-dopa present in skeletal muscle, the effect of insulin on the uptake of L-dopa by skeletal muscle, and the release of L-dopa from skeletal muscle were studied in rats. At all times studied, after L-dopa administration to rats the concentrations of the drug were higher in muscle than in serum or brain. The total amounts of unmetabolized dopa present in muscle were increased by prior insulin administration or carbohydrate consumption: these treatments also increased brain dopa. Of the dopa derived molecules present in various tissues after administration of the amino acid, muscle contained the largest unmetabolized fraction. This finding is compatible with in vitro evidence that muscle contains little catechol-O-methyltransferase or dopa decarboxylase activity and suggests that muscle does not metabolize dopa to a significant degree. Isolated perfused hindquarters taken from rats pretreated with L-dopa released the unmetabolized amino acid into the perfusate; this suggests that when L-dopa concentrations in skeletal muscle exceed those of serum, dopa may also be released into the circulation in vivo. 13 references. (Author abstract modified)

191789 Tarve, U. S.; Paesalu, E. I. Dept. of Biological Chemistry, Tartu Univ., Tartu, USSR **/Amphetamine and Na+,K+ - ATPase in the brain./** Fenamin i Na+, K+-ATFaza mozga. In: Saarma, Yu., Voprosy Klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 148-152). Vol. 9.

The effect of amphetamine on the activity of the Na+, K+ - ATPase of the brain was investigated. In vivo studies were conducted on guinea pigs, and in vitro studies on cat brains. A dosage of 5mg/kg of bodyweight activated Na+, K+ - ATPase but a dosage of 20mg/kg inhibited activity of the enzyme. In vitro studies showed that amphetamine at level of I50=13mM inhibited the activity of Na+, K+ - ATPase. It is suggested that the inhibitory effect resulted from amphetamine's competition with Ka+ in the cell wall. 7 references. (Author abstract modified)

191896 Noon, J. P.; Roth, R. H.; Greengard, P. Yale University School of Medicine, New Haven, CT 06510 **Pharmacological alterations in the stimulus induced release of norepinephrine from the rabbit superior cervical ganglion.** Pharmacologist. 16(2):190, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, pharmacological alterations in the stimulus induced release of norepinephrine (NE-3H) from the rabbit superior cervical ganglion (SCG) were reported. Supramaximal stimulation of the cervical sympathetic nerve caused a frequency dependent increase in the efflux of NE-3H from the superfused rabbit SCG loaded with exogenous NE-3H. Desphenoxybenzamine caused about a 300% increase and phenoxybenzamine about a 400% increase in the stimulated NE-3H efflux from the SCG. This NE-3H efflux was blocked completely by prostaglandin E1 (1 M) and by bretylium. Prostaglandin E2 caused a 50% inhibition and the alpha-adrenergic agonist, methoxamine caused a 70% inhibition of the stimulated NE-3H efflux. These results suggest that NE-3H released upon stimulation of cervical sympathetic nerve occurs from symptathetic terminals in the rabbit SCG and that ganglionic sympathetic terminals are subject to neurosecretory control mechanisms similar to those occurring at sympathetic terminals elsewhere in the peripheral autonomic nervous system. (Author abstract)

191897 Chiueh, C. C.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Amphetamine and methylphenidate induced release of striatal dopamine in vivo: differential effects on 'newley synthesized' and 'stored' pools.** Pharmacologist. 16(2):192, 1974

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, amphetamine and methylphenidate induced release of striatal dopamine in vivo were reported. The cerebral ventricles of anesthetized cats were perfused with artificial cerebrospinal fluid containing purified 3H-tyrosine and the perfusate was analyzed for 3H-catecholamine. The addition of methylphenidate to the 3H-tyrosine solution at the start of perfusion increased the efflux of 3H-dopamine but the methylphenidate response was decreased by 70% when cats were pretreated with reserpine. After reserpine, intravenous injection of increasing doses of d-amphetamine but not of methylphenidate induced an efflux of 3H-dopamine 6-7 fold greater than the content of 3H-dopamine retained in the caudate nucleus. In the central nervous system d-amphetamine and methylphenidate release striatal dopamine from different amine pools, newly synthesized and stored pools, respectively. (Author abstract modified)

191898 Ho, I. K.; Yamamoto, I.; Loh, H. H.; Way, E. Leong. Department of Pharmacology, University of California, San Francisco, CA 94143 **Enhancement of pentobarbital after morphine addiction.** Pharmacologist. 16(2):193, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the responses to pentobarbital in morphine dependence were reported. ICR male mice were rendered dependent on morphine by pellet implantation for 3 days. On administering 75 mg/kg 1.p. sodium pentobarbital, the sleeping time of such animals was found to be more than twofold longer than that of control animals implanted with a placebo pellet. The toxicity of pentobarbital in the morphine tolerant dependent group was also increased, as evidenced by the decrease in LD50 of pentobarbital to 70% of the control group. In morphine pellet implanted mice, the activity of microsomal metabolizing enzyme, as measured by N-demethylation, was 35% inhibited. It appears that the response to pentobarbital is enhanced after chronic morphinization and the effect may be attributed to increased brain uptake of pentobarbital after the development of tolerance and physical dependence on morphine. (Author abstract modified)

191904 Martin, W. R.; Eades, C. G. NIDA Addiction Research Center, Lexington, KY 40507 **Effects of phenethylamine (PEA) in the chronic spinal dog.** Pharmacologist. 16(2):205, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, phenylethylamine (PEA), was studied on the flexor and skin twitch reflexes, pupillary diameter, pulse and respiratory rate and body temperature of the chronic spinal dog. PEA was infused for 12 min at 30 to 72 min intervals. Either saline, chlorpromazine (CPZ) cyproheptadine (CY) or phenoxybenzamine (PB) was administered intravenously between the third and fourth infusion. PEA facilitated the flexor reflex and produced the stepping reflex. It also increased the latency of the skin twitch reflex, dilated pupils, retracted the nictitating membrane and accelerated respiratory rate. CPZ but not CY or PB significantly antagonized the effects of PEA on the flexor reflex, pupillary diameter, skin twitch reflex and nictitating membrane. It appears that although PEA produces effects that are qualitatively similar to those produced by methoxamine, and amphetamine like hallucinogens, its effects can be differentiated from these agents using antagonists, suggesting that the central effects of PEA are not mediated through either a noradrenergic or a tryptaminergic mechanism. (Author abstract modified)

191905 Hollister, A. S.; Ervin, G. N.; Cooper, B. R.; Breese, G. R. Biological Sciences Research Center, UNC School of Medicine, Chapel Hill, NC 27514 **Effects of 6-hydroxydopamine on anorexia produced by d-amphetamine and related phenylethylamines.** Pharmacologist. 16(2):205, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, 6-OHDA was used to destroy selectively brain norepinephrine (NE), dopamine (DA), or both NE and DA containing neurons in male rats. d-Amphetamine produced a dose related decrease in food consumption in control rats, d-amphetamine induced anorexia in animals with brain DA or both DA and NE depleted was significantly reduced or absent. Depletion of brain NE did not alter the anorexic response to d-amphetamine. In contrast to these findings, fenfluramine induced anorexia was not reduced by the 6-OHDA treatments. Results suggest that a brain dopaminergic system mediates d-amphetamine anorexia, but not that caused by fenfluramine. (Author abstract modified)

191906 Tilson, H. A.; Cavanagh, R. L.; Baker, T. G.; Gylys, J. A. Pharmacology Department, Brit Briston Lab., Division of Bristol Myers Co., Syracuse, NY 13201 **Neuropharmacological analysis of R(-)-2,5-dimethyoxy-4-methyl-amphetamine (R-DOM).** Pharmacologist. 16(2):205, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a neuropharmacological analysis of R(-)-2,5-dimethyoxy-4-methyl-amphetamine (R-DOM) was presented. Male, hooded rats were trained to postpone footshock on a signalled continuous avoidance schedule. R-DOM increased response rates and shortened interresponse times. This profile was similar to that produced by most doses of S(+)-amphetamine (A). Larger doses of R-DOM tended to increase the number of shocks while increasing burst and premature responses and decreasing efficient responses. Both alpha-methyltyrosine (MT) and cinanserin (CIN) decreased the rate stimulation produced by R-DOM. MT antagonized the effects of A. CIN enhanced the stimulation of A. Studies of the neurochemical effects of R-DOM indicated dose related increases in the turnover of brain catecholamines, as well as a biphasic effect on the metabolism of serotonin. These data indicate that R-DOM does not affect brain amines uniformly. (Author abstract modified)

191908 Morgenroth, V. H., III; Manion, Albert A.; Roth, Robert H. Yale University School of Medicine, New Haven, CT **Activation of striatal hydroxylase by hydroxylated metabolites of chlorpromazine.** Pharmacologist. 16(2):213, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the activation of striatal tyrosine hydroxylase, (TH) by hydroxylated metabolites of chlorpromazine (CP2) was reported. CPZ had no effect on TH. 7-Hydroxychlorpromazine (7OH-CPZ) produced maximal TH activation (37%). 7, OH-CPZ produced maximal TH activation (62%). Both activations were reversed by addition of calcium (Ca++) to the reaction mixture, even though 7OH-CPZ does not chelate Ca++. 7,8 OH-CPZ altered the kinetics of TH in a fashion similar to EGTA. Other 7,8-dihydroxyphenothiazines were much less effective in activating striatal TH, suggesting that there is some structural specificity involved in the 7,8 OH-CPZ activation.

191918 Walker, C. A.; Charlton, C. G. Department of Physiology and Pharmacology. Tuskegee Institute, Tuskegee, AL 36088 **The effects of amphetamine sulfate on the diurnal rhythms of midbrain; cortex, norepinephrine; serotonin and blood glucose levels in the mouse.** Pharmacologist. 16(2):216, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of amphetamine sulfate on the diurnal rhytmns of midbrain and cortex norepinephrine, serotonin and blood glucose levels in the mouse were reported. Blood glucose levels decreased after 4 hours following amphetamine sulfate treatment. Biphasic changes and serotonin (5-HT) were noted when compared to saline treated controls. When compared to controls the group treated with amphetamine at the hours indicated showed their greatest decrease in blood glucose after 4 hours. In all cases norepinephrine (NE) levels for the amphetamine treated animals peaked at 4 hours following treatment which coincided with blood glucose troughs. An inverse relationship for brain NE and blood glucose existed for at least 16 hours following treatment, but blood glucose and 5-HT showed no clear correlation for the same period. (Author abstract modified)

191920 Anton, A. H.; Gerber, H. R. Department of Anesthesiology, Case Western Reserve Medical School, Cleveland, OH 44106 **A bacterial model for evaluation of barbiturates.** Pharmacologist. 16(2):217, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a bacterial model for evaluation of barbiturates was presented. Only biologically active barbiturates whether hypnotics or convulsants inhibited the E. coli bacteria. Inhibitory activity of the barbiturates increased with lowered pH, suggesting that the unionized fraction was active. No qualitative nor quantitative differences in inhibition were found between the oxygen and sulfur barbiturates. Of the growth factors tried (purines, pyrimidines, nucleic acids, vitamins) only a mixture of amino acids reversed barbiturate inhibition by a nonspecific stimulating effect. Inhibition by barbiturates was removed by a saline wash, suggesting a reversible, physical membrane effect which may be analogous to the mechanism for the hypnotic effect in man. (Author abstract modified)

191921 Cho, A. K.; Hodshon, B. J.; Lindeke, B.; Jonsson, J. Department of Pharmacology, UCLA, Los Angeles, CA 90024 **The 4-hydroxylation of amphetamine and phentermine by rat liver microsomes.** Pharmacologist. 16(2):218, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, sensitive gas chromato-

graphic/mass spectrometric assay was used to measure p-hydroxy-amphetamine and phentermine formation in rat liver microsome preparations. Both amphetamine and phentermine were hydroxylated in the 4 position by an NADP-H dependent system. At higher concentrations, evidence for substrate inhibition was obtained. The reaction is also inhibited by SKF525A, cyanide and nicotinamide. Activity was not increased in microsomes from phenobarbital treated rats. The concentrations of substrates used approximated those found in tissues after pharmacological doses so it is concluded that this system may be responsible for the in vivo biotransformation reaction. (Author abstract modified)

191922 Kuhn, C. M.; Schanberg, S. M. Duke University Medical Center, Durham, NC 27710 **Metabolism of D-amphetamine by rat brain in vivo and in vitro.** Pharmacologist. 16(2):218, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the metabolism of d-amphetamine (A) by rat brain in vivo and in vitro were examined. Concentrations of A, only p-hydroxyamphetamine and p-hydroxynorephedrine (PNE) were identified, but at the higher concentration norephedrine (N) also could be isolated. In addition rats were injected intracisternally with 3H-A, and A and metabolites were isolated at various times after injection. P, N and PNE could be isolated 15 min after injection. While the concentration of P and N declined rapidly over 4 hours the amount of PNE increased gradually during this same period. Brains obtained from animals injected i.p. with the same dose of 3H-A did not contain measurable levels of hydroxylated metabolites. These data suggest that A can be metabolized to P and NE by rat brain tissue. (Author abstract modified)

191923 Miwa, G. T.; Cho, A. K. Department of Pharmacology, UCLA, Los Angeles, CA 90024 **Demethylation of N, N-dimethylamphetamines - evidence for a multienzyme system.** Pharmacologist. 16(2):218, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, evidence for a multienzyme system in the demethylation of N,N-dimethylamphetamines is reported. There was a slight stereochemical preference of about 35% for the (R) over the (S) isomer. Nonlinear regression analysis of the kinetic data favored a double enzyme scheme over a single enzyme model and give rise to significantly different estimates of Vm and Km. Temperature effects, cyanide binding, substrate and product characteristics also support a multienzyme scheme. It is suggested that at least two experimentally distinguishable enzymes are capable of demethylation of this substrate. (Author abstract modified)

191925 Beaubien, A. R.; Mathieu, L. F. Drugs Directorate, Health Protection Branch, Health and Welfare Canada, Ottawa, Canada **Sources of variability in the pharmacodynamics of 14C-imipramine including interaction with diazepam or thioridazine.** Pharmacologist. 16(2):220, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, experiments with orally administered 14C-imipramine done on male Wistar rats to ascertain the important sources of variability in its pharmacodynamics were reported. The results show that the greatest source of variability within groups arises from differences in release of the drug from the stomach. Another important source of variability was in the extent of conversion of imipramine to its metabolites. Diazepam had minimal effects showing only a depression in the ratio of 14C concentration in the small intestinal contents to that of plasma. Thioridazine reduced elimination of radioactivity into bile and urine. These effects of thioridazine appear to be due mainly to a decreased emptying rate of imipramine from the stomach. It is concluded that the stomach is possibly more important than the liver as a site of variability in determining tricyclic antidepressant plasma levels. (Author abstract modified)

191927 Faingold, Carl L. Department of Medical Sciences, Southern Illinois University Medical School, IL **Excitability changes during the gradual development of and recovery from pentylenetetrazol and strychnine induced convulsions in the cat.** Pharmacologist. 16(2):227, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, excitability changes during the gradual development of and recovery from pentylenetetrazol (PTZ) and strychnine (ST) induced convulsions in the cat were reported. Gradual infusion of PTZ and ST induced consistent sequential changes in unanesthetized paralyzed cats resulting in generalized epileptiform paroxysms. Potentials were evoked by auditory, visual, and electrical stimuli and responses were recorded from reticular formation (RF), nonspecific thalamic nuclei and the cerebral cortex. Despite a considerable difference in the nature of the preseizural EEG activity induced by PTZ and ST, several consistent differential evoked response changes were induced by these drugs. Both convulsants enhanced visual and auditory evoked potentials and decreased potentials evoked by RF stimulation. Potentials evoked by thalamic stimulation however, were enhanced by PTZ and depressed by ST. Following seizure the amplitude of the evoked responses remained elevated throughout the remainder of the experiment, up to 7 hours. (Author abstract modified)

191931 Nyback, H. V.; Walters, J. R.; Aghajanian, G. K.; Roth, R. H. Yale University School of Medicine, New Haven, CT 06510 **Noradrenergic neurons: effects of tricyclic antidepressants on single unit activity.** Pharmacologist. 16(2):236, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of tricyclic antidepressants on single unit activity were reported. Tricyclic antidepressants inhibit uptake of norepinephrine (NE) and serotonin (5-HT) into central monoamine neurons. The secondary amine tricyclics are more potent in inhibiting NE uptake and in decreasing NE turnover than those with a tertiary amino group. The latter are more potent in inhibiting 5-HT uptake, in decreasing 5-HT turnover and in depressing firing of 5-HT neurons of the raphe nucleus. The effect of tricyclics on unit activity of NE neurons in the locus coeruleus of the rat was determined by means of extracellular recording techniques. The following order of decreasing potency was found: desipramine, chlordesipramine, imipramine, nortriptyline, amitriptyline, chlorimipramine, iprindole. These results indicate that inhibition of NE uptake facilitates synaptic transmission and induces a feedback inhibition of firing of NE cells. (Author abstract modified)

191932 Goldstein, M.; Lew, J. Y.; Miyamoto, T.; Battista, A. F.; Ebstein, R.; Hokfelt, T.; Fuxe, K. Department of Psychiatry, NYU Medical Center, New York, NY **The localization and characterization of phenylethanolamine-N-methyltransferase activity in specific regions of the CNS.** Pharmacologist. 16(2):236, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the phenylethanolamine-N-

methyltransferase (PNMT) containing neurons in the CNS were examined with immunohistological techniques. Enzymatic activity was found in the C1 and C2 regions of the medulla oblongata, locus ceruleus and in various hypothalamic nuclei. PNMT activity was not detected in the olfactory bulb, caudate and in various cortical areas. 2,3-Dichloro-alpha-methylbenzylamine, a known adrenal PNMT inhibitor effectively inhibits the brain enzyme in vitro and in vivo. Following electrolytic lesions in the C2 area of the medulla oblongata the PNMT activity decreases in various hypothalamic nuclei. Ten to 14 days after hypophysectomy the brain PNMT activity was only slightly decreased. (Author abstract modified)

191933 Shah, Nandkumar S.; Gulati, Om Datt. Ensor Research Lab., William S. Hall Psychiatric Institute, Columbia, SC 29202 **Interactions of psychotropic drugs and mescaline in vitro.** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the interactions between psychotropic drugs and mescaline were examined in vitro rat brain. Imipramine, amitriptyline and nortriptyline reduced the levels of mescaline to about 43% of control. Chlorpromazine (CPZ), stelazine and fluphenazine were about twice as effective as imipramine. Mescaline ratios were unaltered by phenothiazines or antidepressants. Dopamine, dl-norepinephrine (NE), L-dopa, 3,4-dimethoxyphenylethylamine, N-acetylserotonin, 5-methoxytryptamine, ATP, ADP and AMP were ineffective. Data suggest that phenothiazines may permit more of mescaline to act at the receptor site by inhibiting its accumulation and help explain the paradoxical disturbing effects of CPZ when used for the treatment of adverse hallucinogenic reactions. (Author abstract modified)

191936 Goldman, Harold; Fischer, Roland. Ohio State University, Columbus, OH 43210 **Cortical and/or subcortical effects as a function of hallucinogenic drug structure?** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the cortical and subcortical effects of various hallucinogenic drugs were reported. Cross tolerance between lysergic acid diethylamide (LSD) and cyclazocine but none between mescaline and psilocybin was predicted. Even though LSD binds subcortically, its effect on regional perfusion of the brain and, presumably, function is primarily cortical and, since the perfusion shifts evoked by psilocybin are confined to subcortical regions, it is suggested that other compounds with the 2-amino-tetralin structure, such as mescaline, also may selectively affect cortical activity. (Author abstract modified)

191937 McCloskey, Kevin L.; Franz, Donald N. Department of Pharmacology, University of Utah College of Medicine, Salt Lake City, UT 84132 **Effects of LSD, mescaline, and psilocybin on sympathetic preganglionic neurons.** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of lysergic acid diethylamide (LSD), mescaline and psilocybin on sympathetic preganglionic neurons (SPGN) were reported. At doses known to produce behavioral effects, LSD and mescaline routinely enhanced sympathetic discharges in cats whether evoked reflexly by stimulation of spinal afferent fibers or directly by intraspinal stimulation of descending norepinephrine (NE) excitatory pathways. The actions of LSD or mescaline could not be attributed to block of inhibitory 5-hydroxytryptamine (5-HT) receptors although some degree of blockade may have occurred. Rather, the drugs appear to stimulate excitatory NE receptors on SPGNs or to enhance transmission through the excitatory pathways. These results may partially explain the sympathetic stimulation produced by LSD and mescaline in man. Psilocybin routinely depressed evoked sympathetic discharges, possibly by stimulation of inhibitory 5-HT receptors on SPGNs. (Author abstract modified)

191938 Fischer, Roland. Psychiatric Research Center, Box 3235, Baltimore, MD 21228 **Hallucinogens, a re-evaluation.** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a reevaluation of hallucinogens was reported. When central sympathetic arousal is rising, exteroception is transformed into interoception while willed motor activity becomes impaired and inhibited. Hallucinations thus are aroused insights without action and characterized by high interoceptive sensory to motor (S/M) ratios. The 2-amino-tetralin configuration is not restriced to hallucinogenic drugs of the lysergic acid diethylamide (LSD) type and methoxylated amphetamine type but is also a common feature in certain corticosteroids, anesthetics like KetamineR, analgesics, including morphine, and some of its antagonists such as cyclazocine, and isosterically substituted delta9-tetrahydrocannabinol Thus all these drugs which impair reality testing, i.e. raise the S/M ratio, are potential hallucinogens but may only show this effect at toxic dosages. (Author abstract modified)

191942 Parmar, S. S.; Ali, B.; Brumleve, S. J.; De Boer, B. Department of Physiology and Pharmacology, University of North Dakota, School of Medicine, Grand Forks, ND 58201 **Cellular effects of methaqualone on drug metabolizing enzymes.** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of methaqualone (2-methyl-3-o-tolyl-4-quinazolone) on rat liver microsomal drug metabolizing enzymes (MDME) was examined. Single injection of methaqualone inhibited in vivo o-dealkylation of p-nitroanisole while aromatic hydroxylation of aniline was unaltered. Repeated administration of methaqualone for 2, 4 and 8 days caused selective induction of MDME which was 31-41% during o-deaklylation and 12-31% during N-dealkylation of amidopyrine and cocaine. Aromatic hydroxylation was unaltered, while N-dealkylation of morphine was uniformly inhibited up to 67%. These results have indicated that selective induction of hepatic MDME may presumably account for the biochemical basis of the specific drug tolerance by continued methaqualone abuse. (Author abstract modified)

191945 Scholfield, C. N. Department of Psychology, University of Iowa, Iowa City, IA 52242 **Adenosine action on synaptic transmission in brain slices.** Pharmacologist. 16(2):242, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the action of some purines on the electrical activity of slices of guinea pig olfactory cortex were reported. Adenosine, adenosine monophosphate (AMP) or ATP in the bathing solution depressed the negative wave by about 20% increasing to 80% inhibition with increased concentration. Increasing the concentration further produced little further increased depression, suggesting a heterogeneous receptor distribution. The depressed waveforms were unlike those produced by depolarizing agents, gamma-aminobutyric acid or local anesthetics but similar to reducing the stimulus

voltage. Adenine and guanosine had 1/1000th of the potency. Topical application of 1 or 10mM ATP did not produce hyperpolarizations or depolarizations whereas glutamate or raised extracellular potassium concentration generated large extracellularly recorded depolarizations. The depressant action of adenosine suggests that purines may be inhibitory transmitters in brain as has been implicated for gut. (Author abstract modified)

191946 Shih, Tsung-Ming; Khachaturian, Zaven S.; Barry, Herbert, III. Department of Pharmacology, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA 15216 **Evidence for cholinergically mediated effect of methylphenidate hydrochloride in the central nervous system.** Pharmacologist. 16(2):242, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, evidence for cholinergically mediated effect of methylphenidate hydrochloride in the central nervous system was reported. Intravenous injection of methylphenidate HCl (MPH) significantly attenuates single unit activity (UA) in the collateral sensory pathways of the mesencephalic reticular formation (MRF) in immobilized rats. This effect of MPH was mimicked by the cholinergic stimulants, nicotine and oxotremorine. The effect of MPH was abolished by the nicotinic blocker, mecamylamine HCl but was not affected by the muscarinic blocker, atropine sulfate. The attenuation of UA was only slightly reduced when catecholamines and serotonin were depleted by pretreatment with reserpine at 24 and again at 18 hours before or with tetrabenazine at 3 hours before MPH or OXO. These results suggest that inhibitory effects of MPH in the collateral sensory pathways of the MRF might be mediated by the cholinergic system. (Author abstract modified)

191948 Svensson, Torgny H.; Bunney, Benjamin S.; Aghjanian, George K. Yale University School of Medicine, New Haven, CT 06508 **Noradrenergic regulation of brain serotonergic neurons: evidence from single unit studies with clonidine.** Pharmacologist. 16(2):244, 1974.

At the fall meeting of the American Society for Pharmacology and Exeprimental Therapeutics, the effects of clonidine on the firing rates of brain noradrenaline (NA) neurons in locus coeruleus and serotonergic (5-HT) neurons in raphe dorsalis by means of single cell recording were reported. NA neurons and a majority of 5-HT neurons were inhibited by clonidine. The effect on the 5-HT neurons seems to be secondary to the effect on the NA neurons since destruction of the NA input by pretreatment with intraventricularly administered 6-hydroxydopamine abolished the effect of clonidine on the raphe. The NA releasing drugs, d or l-amphetamine reversed the effect of clonidine on the raphe. The results support the contention that brain NA neurons may exert a regulatory influence on 5-HT neurons in the raphe. (Author abstract modified)

191949 Gallager, D. W.; Aghajanian, G. K. Yale University School of Medicine, New Haven, CT 06510 **Chlorimipramine and LSD: differential effects on the in vivo release of 3H-5HT.** Pharmacologist. 16(2):244, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the differential effects of chlorimipramine (CIM) and lysergic acid diethylamide (LSD) on the in vivo release of 3H-5-hydroxytryptamine 3H-5HT were reported. Although CIM or LSD both inhibit raphe cell firing for about 1 hour, th efflux cH-5HT is affected differentially by the two drugs. Chlorimipramine produces either an increase or no change in the efflux of 3H-5HT. In contrast, LSD at both 100 and 200mg/kg produces a decrease in 3H-5HT efflux. These results show that although the effects of CIM and LSD on 5HT turnover and raphe neuronal firing are similar, distinct differences in their actions are revealed by measuring the efflux of 3H-5HT. (Author abstract modified)

191950 Couch, J. R. Kansas City University Medical School, Kansas City, KS **Blockade of excitatory 5HT synapse by LSD.** Pharmacologist. 16(2):244, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the blockade of an excitatory 5-hydroxytryptamine (5HT) synapse by lysergic acid diethylamide (LSD) was reported in the raphe nucleus. Of 33 D cells identified, all responded to 5HT with excitation. Responses to LSD were minimal. In 10 neurons, iontophoretically applied LSD simultaneously blocked or partially blocked excitation by iontophoresed 5HT and by nucleus paragigantocellularis lateralis (NPL) stimulation. Intravenous LSD blocked or partially blocked iontophoresed 5HT and synaptic stimulation in 5 of 6 additional cells. dl-Homocysteic acid (DLH) was iontophoresed and demonstrated the cells were still excitable while under LSD block. LSD blocked synaptic and iontophoretic responses in only 1 of 5 cells. For all cells tested for 5HT-LSD interactions, LSD blocked 5HT excitation in 19 of 20, but blocked 5HT inhibition in only 5 of 15. LSD appears to block preferentially 5HT excitatory synapses. (Author abstract modified)

191951 Bymaster, Franklin P.; Wong, David T. Lilly Research Labs., Indianapolis, IN 46206 **Effect of Lilly 110140, 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine on synthesis of 3H-serotonin from 3H-tryptophan in rat brain.** Pharmacologist. 16(2):244, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of Lilly 110140, 3-(p-trifluoromethylphenoxy)-N-methyl-3-phenylpropylamine on synthesis of 3H-serotonin (5-HT) from 3H-tryptophan (3H-TP) was reported. The administration of Lilly 110140 at 10mg/kg reduced the synthesis of 3H-5HT from 3H-TP of normal rats. The formation of 5HIAA contents in brains were also reduced in a dose dependent manner. The effect of 3H-5HT, 3H-5HIAA and total 5HIAA were most pronounced in cerebral cortex and brain stem. It is suggested that the decrease in synthesis of 3H-5HT and 3H-5HIAA from 3H-TP was due to the decrease in the firing of serotoninergic neurons upon selective inhibition of 5HT uptake by Lilly 110140 without an inhibition of TP uptake. (Author abstract modified)

191955 Ervin, G.; Cooper, B. R.; Breese, G. R. Biological Sciences Research Center, University of North Carolina Medical School, Chapel Hill, NC 27514 **Effects of various drugs on the actions of 5,7-dihydroxytryptamine.** Pharmacologist. 16(2):249, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of various drugs on the actions of 5,7-dihydroxytryptamine (5,7-DHT) were reported. It was found that prior administration of pargyline or other monamine oxidase inhibitors blocked the reduction of brain norepinephrine by 5,7-DHT, while permitting the usual depletion of serotonin (5-HT) content. Depletion of 5-HT was further increased by administering an additional treatment with pargyline and 5,7-DHT. Serotonin content was reduced by approximately 75% at the end of 30 days as compared with 60% in animals that received only a single treatment. These findings indicate that pretreatment of animals with pargyline or desipramine can be used to increase the

specificity of 5,7-DHT on 5-HT fibers. (Author abstract modified)

191956 Arora, R. C.; Vugrincic, C.; Ungar, F.; Alivisatos, S. G. A. Department of Biochemistry, Chicago Medical School, Chicago, IL 60612 **The presence of MAO in synaptic membranes of bovine brain.** Pharmacologist. 16(2):249, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the presence of monoamine oxidase (MAO) in synaptic membranes was reported. Synaptic membranes were isolated by the modified procedure on discontinuous sucrose gradients and ficoll gradients. Greater MAO activity was found in mitochondria as compared to end synaptic membranes. Their activity was differentiated by the use of specific inhibitors, i.e. clorogyline and deprenil, for the enzyme A and B. Treatment of the fractions with organic solvent increases the specific activity of membranes while there is no change or decrease in the specific activity of mitochondria. These results support the presence of a specific type of MAO in synaptic membranes in addition to that of mitochondria. (Author abstract modified)

191960 Levy, J. A.; Munson, A. E.; Harris, L. S.; Dewey, W. L. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Effects of delta8 and delta9 tetrahydrocannabinol on the immune response in mice.** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, skin graft survival (BDF skin on NYLAR mice) was determined following treatment with delta8 and delta9 tetrahydrocannabinol (THC) bound to bovine serum albumen (BSA). THC increased graft survival time 21% to 42% over controls. In studies to determine the effect of delta8 and delta9-THC on IgM response to sheep erythrocytes (sRBC), drugs were administered orally with and for 7 days following i.p. injection of 0.1ml of 20% suspension of sRBC. Delta9-THC reduced the hemagglutanin titer 72% as compared to controls. Similar results were obtained for delta8-THC. Treatment of mice with Delta9-THC daily for 7 days did not alter the functional activity of the reticuloendothelial system as measured by the vascular clearance of colloidal carbon. (Author abstract modified)

191962 Nagle, Barbara T.; DiGregorio, G. J.; Chernick, W. S. Hahnemann Medical College, Philadelphia, PA 19102 **The influence of delta-9-tetrahydrocannabinol (THC) on pilocarpine (PILO) induced parotid secretions of the rat.** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, total flow, total amylase and meq/l of sodium, potassium and calcium ions of induced parotid secretions of male Wistar rats were determined following administration of tetrahydrocannabinol (THC) or the ethanol (ETOH) vehicle. Parotid secretions were induced by i.a. infusion of pilocarpine (PILO) for 20 minutes. THC and ETOH failed to alter the total flow of the induced secretions as compared to the PILO controls (PC). The higher dose of THC significantly increased the amylase concentration as compared to PC and the ETOH group. Neither dose of THC caused an alteration of any of the ion concentrations monitored. Since there was no alteration of secretory flow, yet a marked increase in amylase, it is concluded that THC exerts an influence on parotid secretions independent of its cardiovascular effects (decrease in blood pressure and heartrate). (Author abstract modified)

191963 Harris, L. S.; Munson, A. F.; Friedman, M. A.; Dewey, W. L. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Retardation of tumor growth by delta9-tetrahydrocannabinol (delta9-THC).** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the oral administration of delta9-tetrahydrocannabinol (THC) bound to bovine serum albumin was investigated for potential antitumor action on Lewis lung carcinoma. On day 12 of this experiment, THC retarded primary tumor growth 48%, 72% and 75%. Mice receiving 100mg/kg survived 36% longer than control as compared to 45% for the cyclophosphamide positive control. Mice treated for 20 days showed slightly less inhibition of primary tumor growth with no increase in lifespan. Cannabinol, at the same doses as THC, administered for 20 days showed slightly less activity on tumor growth and did not prolong survival time. In preliminary mechanismistic studies, THC administered acutely, inhibited 3H thymidine uptake into tumor DNA but not in brain, testes, spleen or bone marrow. Twenty four hours after a single oral gavage of 400mg/kg THC, DNA synthesis was reduced 75%. DNA synthesis was not significantly altered in primary tumor or tissues of mice similarly treated for 20 days. (Author abstract modified)

191964 Howes, J. F.; Osgood, P. P. Sheehan Institute and Sharps Associates, 767-B Concord Ave., Cambridge, MA 02138 **The effects of delta9-THC and a water soluble derivative on PGE1 synthesis in the corpus striatum.** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of delta9-tetrahydrocannabinol (THC) on prostaglandin synthesis was reported. Preparations of the corpus striatum of rats, possess prostaglandin (PGE1) synthetic activity and this activity may be enhanced by the addition of ADP. The inhibition of normal and adenosine diphosphate induced synthesis of PGE1 by THC, a derivative ((-)-trans-delta9-tetrahydrocannabinol-4-(morpholino)butyrate hydrobromide and indomethacin. (Author abstract modified)

191965 Thompson, G. R.; Rosenkrantz, H.; Fleishman, R. W.; Braude, M. C. Mason Research Institute, Worcester, MA **Effects of delta-9-tetrahydrocannabinol (delta-9-THC) administered subcutaneously to rabbits for 28 days.** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, subcutaneous administration of delta9-tetrahydrocannabinol (THC) to rabbits produced dose related cumulative toxicity. Dose related dermal responses included erythema, edema, ulceration and nodule formation. Some of the granulomatous nodules contained an oily substance and exhibited liquefactive necrosis. The severities of erythema and ulceration were generally maximal during the first week of treatment, but edema and nodule formation were most severe after days 12 and 14, respectively. All rabbits survived treatment, but bodyweights, liver weights and liver glycogen were decreased in a dose related manner. Gross pathology of organs was essentially negative. (Author abstract modified)

191968 Dewey, W. L.; Martin, B. R.; Harris, L. S.; Beckner, J. S. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Disposition of H3-delta9-tetrahydrocannabinol in brain of pregnant dogs and their fetuses.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the amount of labelled tetrahydrocannabinol (THC) that accumulates in rat brain was reported. The radioactivity in the brain of mothers was located primarily in the crude mitochondrial fraction (45%), while the rest was distributed among the crude nuclear (24%), microsomes (11%) and supernatant fractions (15%). The distribution of radioactivity in the fetal brains differed markedly from that in the maternal brains. In the fetal brains, the crude mitochondria contained only 19%, whereas the microsomes and the supernatant contained 22 and 32%, respectively. A positive correlation was found between the distribution of radioactivity and phospholipid content in fetal and maternal brains. (Author abstract modified)

191969 Williams, B. I.; Nash, J. B.; Pirch, J. H. Department of Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX 77550 **Distribution of 14C-delta9-THC in male and female rats.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the distribution of 14C-delta9-tetrahydrocannabinol (THC) in male and female rats was reported. The radiolabeled extract was administered i.v. to six male and six female rats in a dose of THC of 2mg/kg. Forty five min after drug administration, levels of radioactivity of THC and metabolites were significantly higher in brain, liver, muscle, and plasma of female than of male rats. The higher concentration of THC and or metabolites in the brain of females may account for their greater behavioral response to marihuana extract. (Author abstract modified)

191970 Martin, B. R.; Dewey, W. L.; Harris, L. S.; Beckner, J. S. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Subcellular localization of H3-delta9-tetrahydrocannabinol in dog brain after acute or chronic administration.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, to ascertain if an alteration in the cellular or subcellular localization of tetrahydrocannabinol (THC) in brain is responsible for tolerance, dogs received either one IV injection of 0.5mg/kg of H3-THC or six daily IV injections of 0.5mg/kg of THC followed by an injection of H3-THC. The pattern of distribution of radioactivity was similar for both groups of dogs. The greatest amount of radioactivity was in rostral and caudal colliculi, pituitary, hippocampus, thalamus, and geniculate bodies. Radioactivity in the gray matter of the cerebral cortex and cerebellum was 70.4DPM/mg of tissue, whereas only 38.1DPM/mg was found in the white matter. The localization of radioactivity in the subcellular fractions was similar for both groups. The subcellular localization for the cerebral cortex was as follows: crude nuclear fraction (20%), crude mitochondrial (45%), microsomal (11%), and supernatant (14%). (Author abstract modified)

191971 Adams, M. D.; Dewey, W. L.; Harris, L. S. Medical College of Virginia, Richmond, VA 23298 **Cardiovascular effects of delta8- and delta9-tetrahydrocannabinol in rats.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the cardiovascular effects of delta8 and delta9-tetrahydrocannabinol (THC) were reported. Intraarterial injections of delta8 and delta9-THC produced vasoconstriction in the perfused hindquarters of rats. Dose response curves indicate that delta8 and delta9-THC have equal potency with regard to this vasoconstrictor action. The hindquarter vasoconstrictor response to delta9-THC was not altered by treatment with phenoxybenzamine. Constrictor responses to delta9-THC were also measured before and after phentolamine. These data illustrate that delta8 and delta9-THC may have vasoconstrictor actions in certain vascular beds which may be independent of stimulation of alpha adrenergic receptors. (Author abstract modified)

191984 Cooper, B. R.; Ervin, G.; Breese, G. R. Biological Science Research Center, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **A role for dopamine in the stimulant effects of amphetamine on locus coeruleus self-stimulation.** Pharmacologist. 16(2):308, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a role for dopamine in the stimulant effects of amphetamine on locus coeruleus (LC) self-stimulation was described. Following a 24 hr pretreatment with reserpine to eliminate stores of amines, rats were given either L-alpha-methyl-tyrosine (MT) to block catecholamine synthesis or of the dopamine-beta-hydroxylase inhibitor U-14,624, to block norepinephrine (NE) synthesis. When d-amphetamine was given 1 hr after these synthesis inhibitors, vehicle and U-14624 treated rats from the LC and substantia nigra (SN) groups displayed a marked increase in responding to d-amphetamine. Rats given MT did not respond after the d-amphetamine treatment. Results suggest that DA neural systems are implicated in the effects of d-amphetamine on self-stimulation even when electrodes are placed in the LC which contains NE cell bodies. (Author abstract modified)

191985 Bhargava, Hemendra N.; Way, E. Leong. Department of Pharmacology, University of California, San Francisco, CA 94143 **Morphone tolerance, dependence and withdrawal and brain acetylcholine.** Pharmacologist. 16(2):270, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the relationship between morphine tolerance, dependence and withdrawal and brain acetylcholine (ACh) was examined in rats. Mice and rats rendered morphine tolerant dependent (M) by implantation of one and four pellets, respectively, for 3 days showed increased brain ACh. Six hr after pellet removal from M mice, this increase was even higher. Brain ACh levels returned to normal beyond 12 hr after abrupt withdrawal. Pellet removal from M rats did not affect brain ACh. Administration of naloxone (N) increased brain ACh in naive mice but decreased in M mice and rats. This decrease in brain ACh in M animals was observed only in those that jumped after N and not in those that failed to jump. Brain choline levels were unchanged by the above treatments. It appears that N induced withdrawal jumping in M animals is associated with an enhanced ACh release. (Author abstract modified)

191988 Alderman, J. L.; Shellenberger, M. K. Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS 66103 **The effect of increased gamma-aminobutyric acid on alpha-methyltyrosine induced decrease in catecholamines in rat brain.** Pharmacologist. 16(2):272, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of increased gamma-aminobutyric acid (GABA) on catecholamine (CA) metabolism was determined. Female haltzman rats were pretreated with the GABA transaminase inhibitor, hydrazino propionic acid (HPA) and subsequently (0 hr) with alpha-methyltyrosine (AMT). Novepinephrine (NE), dopamine (DA), and GABA were measured in the cortex, cerebellum, midbrain, medulla, and striatum. When HPA + AMT animals were compared to saline + AMT controls, no significant al-

terations were observed in the rate of NE decrease in any area, nor in the rate of DA decrease, except in the striatum, where the rate of DA decrease was significantly depressed after HPA. A relatively specific interaction between GABA and striatal DA is suggested. (Author abstract modified)

191992 Consroe, Paul F.; Jones, Byron; Picchoni, Albert; Chin, Lincoln. Department of Pharmacology and Toxicology, University of Arizona College of Pharmacy, Tuscon, AZ 85721 **Neuropharmacological analysis of central adrenergic and cholinergic antagonism of delta9-tetrahydrocannbinol.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, interactions between delta9-tetrahydrocannabinol (THC) and methamphetamine, an adrenergic agonist, and between THC and physostigmine, a cholinomimetic, were assessed by measurement of electroencephalographic (EEG) and behavioral changes in unrestrained adult rabbits. The increase in cortical electrogenesis (EEG voltage output) induced by THC was reversed by both methamphetamine and physostigmine. Disruption of the hippocampal theta rhythm induced by THC was restored by methamphetamine and physostigmine. Both drugs also antagonized THC induced sprawling and suppression of exploratory activity. THC and methamphetamine interacted synergistically and produced pathological behaviors. There was little evidence of behavioral toxicity associated with the THC-physostigmine combination. These results indicate that methamphetamine or physostigmine can antagonize many effects of THC, but that behavioral toxicity may results from interaction of THC and adrenergic agents. (Author abstract)

191994 Cely, William; Turkanis, Stuart A.; Karler, Ralph. Department of Pharmacology, University of Utah School of Medicine, Salt Lake City, UT 84132 **Anticonvulsant properties of cannabidiol.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, cannabidiol was subjected to a series of standard anticonvulsant tests with mice so that its properties could be compared with those of other agents, such as delta9-tetrahydrocannabinol (THC) and diphenylhydantoin (DPH). Anticonvulsant doses of CBD were observed to lower body temperature at an ambient temperature of 22 degrees but at 30 degrees C the hypothermia was minimized. At both ambient temperatures, CBD abolished hindlimb extension induced by maximal electroshock (MES) and raised the MES (extensor) and the 6-Hz-electroshock thresholds but did not affect either the 60-Hz-electroshock threshold or minimal seizures caused by pentylenetrazol. Thus hypothermia produced by CBD does not appear to influence the anticonvulsant properties of the drug. The results indicate that CBD exhibits anticonvulsant characteristics more closely related to DPH than to THC. (Author abstract modified)

191995 Hancock, John C.; Wise, Judy G. Department of Pharmacology, Louisiana State University, Medical Center, New Orleans, LA 70112 **Effects of amphetamines on molluscan neurons.** Pharmacologist. 16(2):280, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of dextroamphetamine (DAMPHET) were studied on identified neurons in the visceral ganglion of Helix pomatia. On dopaminoceptive (DA) cells DAMPHET caused a depolarization, increased firing rate and a decreased input resistance. These effects were selectively blocked by dihydroergotamine. On cholinoceptive (Ch) cells DAMPHET caused a depolarization, increased firing rate and a decreased input resistance. These effects were selectively blocked by d-tubocurarine. Increasing the magnesium (Mg) concentration from 4 to 20 mM blocked orthodromic stimulation, spontaneous excitatory postsynaptic potentials and depressed postjunctional drug effects. Elevating Mg, caused a greater depression of the response to DAMPHET than to epinephrine or norepinephrine. This suggests that DAMPHET has both prejunctional and postjunctional effects on DA cells. (Author abstract modified)

191996 Segal, M.; Cochin, J. Boston University School of Medicine, Boston, MA 02118 **Delta9-tetrahydrocannbinol (delta9-THC)-imipramine interaction on mouse body temperature.** Pharmacologist. 16(2):282, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the interaction of imipramine (Im) and delta9-tetrahydrocannbinol (THC) at varying ambient temperatures was reported. Mice were placed in a controlled temperature chamber and were given THC 1 hour before Im. At 30 degrees C the Im induced hyperthermia was blocked by THC; at 20 degrees C the Im induced hypothermia was enhanced by THC. The interaction between THC and imipramine at controlled ambient temperature may shed some light on the mechanism of impramine's action on temperature. (Author abstract modified)

191997 Aroura, Satish; Hardman, Harold F. Medical College of Wisconsin, Milwaukee, WI 53233 **Analysis of hypothermic action of delta9-tetrahydrocannabinol (delta9-THC) in mice.** Pharmacologist. 16(2):282, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the hyperthermic action of delta9-tetrahydrocannabinol (THC) was reported. The hypothermic effect of THC was monitored by simultaneous measurement of deep rectal, flank and tail temperatures. Graded doses of THC were administered i.v. at ambient temperatures of 10 degrees and 20 degrees C. The fall in tail temperature is progressively reduced whereas the fall in deep rectal temperature is progressively increased with graded doses of THC. Heat conservation mechanisms appear to be operative and hypothermia may result primarily from decreased heat production. (Author abstract modified)

191998 Freidman, E.; Gershon, S. New York University School of Medicine, New York, NY 10016 **Tetrahydrocannabinols: inhibition in acetylcholine synthesis in regional rat brain slices.** Pharmacologist. 16(2):286, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of acute and chronic treatment with tetrahydrocannabinols (THC) on brain acetylcholine synthesis were studied in male albino rats. A dose related inhibition in striatal, hypothalamic, and cortical acetylcholine synthesis was obtained with acute 5-20mg/kg doses of delta8-THC and delta9-THC. Chronic treatment with delta9-THC for 5 days did not result in tolerance to the effect. Acute and chronic treatments with delta9-THC did not alter striatal choline acetyltransferase activity. Treatment with the tetrahydrocannabinols did not alter synaptosomal uptake of choline. The inhibition of brain acetylcholine synthesis by the tetrahydrocannabinols can be reversed by in vitro potassium depolarization. It is concluded that THC induced inhibition of acetylcholine synthesis is related to a decrease in cholinergic neuronal activity. (Author abstract modified)

191999 Simon, Jay R.; Kuhar, Michael J. Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Inhibi-**

tion of choline uptake into synaptosomes by choline analogues. Pharmacologist. 16(2):286, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the inhibition of the high affinity uptake of choline into synaptosomes by several choline analogues was studied. Hemicholinium-3 (HC-3), triethylethanolamine (TEE), trimethylpropanolamine (TMP), acetylcholine (Ach), thiocholine (TIO), and N,N-dimethylethanolamine were the most potent inhibitors of those compounds examined, but exhibited a very wide range (2000-fold) of inhibitory potency. The inhibition due to these compounds was examined by kinetic analysis and exhibited competitive kinetics. HC-3 was the most potent inhibitor. TEE and TMP were the next potent. The relatively poor inhibitory potency of TIO and Ach suggest that these two compounds have a lower affinity for the uptake site and thus would not be transported very efficiently by the choline uptake mechanism. These findings suggest that alterations on the choline quaternary nitrogen rather than the hydroxyl group may result in new compounds that are potent uptake inhibitors or perhaps form false transmitters. (Author abstract modified)

192000 Barker, L. A.; Mittag, T. W.; Glick, S. D.; Matriano, D.; Tormay, A.; Crane, A. Mt. Sinai School of Medicine, CUNY, New York, NY 10029 **Analogs of choline: synaptosomal metabolism.** Pharmacologist. 16(2):286, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the analogs of choline in synaptosomal metabolism were examined. Monoethylcholine (MEC) and N-hydroxyethyl pyrrolidinium methiodide (Pyrrol-Ch) are substrates for rat forebrain choline acetyltransferase; Km's are 1.26 and 6.65 mM and Vm's relative to choline are 1.02 and 0.53 respectively. (3H)Choline, (3H)MEC and (3H)Pyrrol-Ch are transported into synaptosomes by the high affinity system. Vmaxs relative to choline are 1.00 for both MEC and Pyrrol-Ch. Choline inhibits the transport of (3H)MEC and (3H)-Pyrrol-Ch. As a percent of the total amount transported, all are converted to the same extent (ca 45%) to their respective acetyl derivatives. The observations support the hypothesis that the high affinity transport of choline can be rate limiting in the biosynthesis of acetylcholine. (Author abstract modified)

192001 Haubrich, Dean R. Squibb Institute of Medical Research, Princeton, NJ 08540 **Inhibition in vivo of acetylcholine synthesis in mouse brain by inhibitors of choline acetyltransferase.** Pharmacologist. 16(2):286, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the in vivo inhibition of acetylcholine synthesis by inhibitors of choline acetyltransferase in the mouse brain was reported. Inhibition in vitro by juglone (5-hydroxy-1,4-naphthoquinone) of choline acetyltransferase (CAT) in rabbit brain was competitive for acetyl-CoA, noncompetitive for choline (Ch), and not reversible by dialysis. Administration of juglone to mice increased the uptake of Ch (3H) by brain but had no effect on either the amount of radioactive acetylcholine (ACh) formed or the endogenous concentration of Ch or ACh in brain, suggesting that juglone inhibits brain ACh synthesis in vivo. Administration of the CAT inhibitor naphthylvinyl pyridine also failed to alter the endogenous concentration of Ch or ACh in mouse brain, but did reduce the amount of ACh synthesized from Ch (3H). These findings suggest that inhibition in vivo of ACh synthesis in brain by a CAT inhibitor need not be accompanied by a reduction in concentration of the reaction product, ACh. (Author abstract modified)

192003 Vetulani, J.; Dingell, J. V.; Sulser, F. Vanderbilt University School of Medicine, Nashville, TN 37232 **Effect of chronic treatment with desipramine (DMI) and iprindole (IP) on the norepinephrine (NE) sensitive adenylate cylase system in slices of the rat limbic forebrain.** Pharmacologist. 16(2):287, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of desimipramine (DMI) and iprindole (IP) following chronic administration on the norepinephrine (NE) sensitive cyclic adenosine monophosphate (AMP) generating system in LFS and on behavior in open field tests (OFT) were reported. NE caused a consistent increase of the nucleotide to 180-240% of control values. While a single dose of DMI or IP did not alter the cyclic AMP response to NE, treatment for 7 to 16 days lead to increased responses in some but not all the animals. In the OFT, rearing and emotional defecation were significantly increased. Between 4 and 8 weeks of treatment, the cyclic AMP response to NE in LFS and ambulation in the OFT were significantly reduced. The levels of the drugs in brain were similar at early and late times. The results suggest that the antidepressant action of tricyclics may be related to postsynaptic changes in the sensitivity of the adenylate cyclase system to NE rather than to their action on presynaptic sites. (Author abstract modified)

192006 Gessner, Peter K. Pharmacology Department, State University of New York at Buffalo, Buffalo, NY 14214 **Induction of a diethyl ether withdrawal syndrome in mice by exposure to ether vapor.** Pharmacologist. 16(2):304, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the induction of a diethyl ether withdrawal syndrome in mice by exposure to ether vapor was reported. Mice were exposed to ether vapor for a period of 3 days. At the end of this period the 22 experimental and the 10 control mice were individually isolated using a double-blind procedure and withdrawal signs were scored. Withdrawal seizures were observed in 13 of the 22 ether exposed mice. Seizure scores reached near maximum values within 30 min of withdrawal, plateaued at this level for the next 4 hrs and then decreased gradually over the next 20 hrs. It was found that ether withdrawal seizures were surpressed by administration of either ethanol or phenobarbital to the withdrawn animals. The results raise the possibility of the existance of cross-physical dependence between ether and agents such as ethanol and phenobarbital. (Author abstract modified)

192020 Siemens, A. J.; Kalant, H. Department of Pharmacology, University of Toronto, Toronto 181, Canada **Metabolism of delta1-tetrahydrocannabinol by rats tolerant to marihuana.** Pharmacologist. 16(2):327, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the metabolism of delta1-tetrahydrocannabinol (THC) by rats tolerant to marihuana was examined. Adult male Wistar rats treated daily with a marihuana extract (ME) providing THC did not gain weight for 7 days but then became tolerant to this initial effect and gained at the same rate as controls. After 28 days of treatment, neither the rate of THC metabolism nor the formation of its metabolites by liver preparations was altered compared to controls. Other rats treated 14 days with another ME became tolerant to a THC mediated prolongation of ethanol sleeping time. The rates of biliary excretion and disappearance from the blood and tissues (disposition) of THC and its metabolites were not altered. But THC metabolism was induced by phenobarbital (PB) treatment. The rate of formation

in vitro of highly polar metabolites of THC was increased while the final concentration of 7-hydroxy-THC was decreased compared to controls. The rate of disposition of THC was also increased significantly in vivo by PB treatment. Tolerance to marihuana in the rat is more likely of CNS than of dispositional origin. (Author abstract modified)

192335 Karoum, F.; Wyatt, R.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Estimation of the contribution of peripheral and central noradrenergic neurones to urinary 3-methoxy-4-hydroxyphenylglycol in the rat.** Neuropharmacology (Oxford). 13(3):165-176, 1974.

A method that differentially measured the contribution to urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) formation made by noradrenergic neurones in the peripheral sympathetic nervous system (PSNS) and in the central nervous system (CNS) of the rat is described. Reasons for the choice are listed. The method to estimate central and peripheral contribution is used in normal rats and in rats who received 6-hydroxydopamine (6-OHDA) intravenously and intraventricularly. While 24 h excretion of MHPG failed to reflect the expected reduction in brain norepinephrine (NE) metabolism after administration of 6-OHDA intraventricularly, the measurement of central and peripheral contribution to urinary MHPG was found to yield results consistent with the expected decrease of NE metabolism following intravenous or intraventricular administration of 6-OHDA. 52 references. (Author abstract modified)

192413 Willinsky, M. D.; Webster, C. D.; Herring, Barbara S. Department of Pharmacology, University of Toronto, Toronto, Ontario, Canada **Effects of delta1-tetrahydrocannabinol on Sidman discriminated avoidance behavior in rats.** Activitas Nervosa Superior (Praha). 16(1):34-38, 1974.

Data on the dose - effect relationship of delta1-tetrahydrocannabinol (THC) as an hallucinogen were studied in rats. There were increases in premature and late responding though both effects did not always occur. The drug did disrupt discrimination; on the basis of nonavoidance from predrug day to postdrug day, there appeared to be a dose response curve over the dose range 0.75 to 96 mg/kg THC. The fact that both the premature and the late effect was not found in 21 cases indicates that THC can be only tentatively classified as an hallucinogen according to Smythies' scheme. 5 references.

192416 Szekely, J. I.; Borsy, J.; Kiraly, Ildiko. Research Institute for Pharmaceutical Chemistry, Budapest 4, Szabadsagharcosok u. 47-49, Hungary **Chlordiazepoxide induced beta spindle activity in rats.** Activitas Nervosa Superior (Praha). 16(1):44-46, 1974.

Additional material for the electrophysiology of chlordiazepoxide in rats was obtained. Following chlordiazepoxide administration, two types of fast spindle activity appeared in the epidural leads. Large slow waves appeared in the subcortical structures. Only the spindles of great amplitudes and slower frequency spread over the hippocampus but very rarely over the reticular formation. The action of the drug is mediated through the limbic system. 13 references.

192423 Bickel, M. H. Medizinisch-chemisches Institut, University of Berne, Berne, Switzerland **True and apparent non-penetration of the blood brain barrier by psychotropic drugs.** Activitas Nervosa Superior (Praha). 16(1):60-62, 1974.

Cases of polar drugs penetrating and lipophilic drugs not penetrating the blood-brain barrier are presented. Selective passage of imipramine and its metabolites into the brain was studied. The appearance and nonappearance of desmethylimipramine were examined in rat brains treated with imipramine. 15 references.

192425 Hopf, A.; Eckert, H. Institute f. Hirnforschung, Univ. Dusseldorf, Himmelgeister Str. 300/5, 4 Dusseldorf, Germany **Distribution of 14C-psilocin in the brains of various animals.** Activitas Nervosa Superior (Praha). 16(1):64-66, 1974.

The distribution patterns of neuroleptics, antidepressants, and hallucinogens within rat brain were studied in rats. A determination was made of whether or not various psychoactive drugs showed common distribution patterns in different species. Correlations were studied between the distribution of the drugs and their morphological, histochemical, or chemical patterns. 3 references.

192426 Keating, J.; Guerra, F. C.; Burton, R. M. Centro de Estudos de Bioquimica, Instituto do Alto Cultura, Faculdado de Farmacia, Porto, Portugal **Incorporation of 14C-dihydrophenylalanine and 14C-choline into rat brain subcellular particles and the effect of psychoactive drugs.** Activitas Nervosa Superior (Praha). 16(1):66-68, 1974.

The incorporation of radioactive precursors into brain amines and the distribution pattern in brain subcellular particles were studied in rats. Changes induced by psychoactive drugs (reserpine, chlorpromazine trifluopenazine) were observed. The subcellular distribution patterns of brain amines can be measured by the incorporation of radioactivity from precursors, such as 14C-choline and 14C-DOPA, into the subcellular fractions of brain. Preliminary experiments indicated that more detailed information concerning the mechanisms of action of psychoactive drugs may be obtained by studying the drug induced alteration of brain subcellular patterns of distribution of neurotransmitter amines. 6 references.

04 MECHANISM OF ACTION: BEHAVIORAL

187258 Langfeldt, Thore. Institute of Neurophysiology, University of Oslo, Karl Johansgt. 47, Oslo 1, Norway **Diazepam-induced play behavior in cats during prey killing.** Psychopharmacologia (Berlin). 36(2):181-184, 1974.

Diazepam induced play behavior in cats during prey killing is reported. Cats exhibiting prey killing were divided into two categories by the appearance of prey - play behavior: immediate killers that never exhibited prey - play behavior and delayed killers that always exhibited play behavior prior to the mortal neckbite. Low doses of diazepam given to immediate killers induced prey - play behavior and higher dosages increased the play period. The significance of the play behavior and possible underlying mechanisms of the drug action are discussed. 6 references. (Author abstract)

187259 Van der Poel, A. M. Department of Fundamental Pharmacology, University of Leiden, Wassenaarseweg 62, Leiden, The Netherlands **The influence of 3-quinuclidinylbenzilate on the behaviour of rats in a circular runway.** Psychopharmcologia (Berlin). 36(2):151-162, 1974.

The influence of 3-quinuclidinylbenzilate on the behavior of rats was studied. Thirty six female albino rats, trained to run for a chocolate reward in a circular runway, were treated according to 6 X 6 Latin square schemes with five doses of 3-quinuclidinylbenzilate, or the vehicle. The drug caused a

marked, dose dependent increase of the latency, whereas the effect on running time was comparatively small. During the latency the frequency of ambivalent behaviors, shown at the transition of the start - goal compartment and the runway, increased under the influence of 1mg/kg or more. Concomitant increases were noted in the frequency of displacement activities, which were absent in control animals. The results were interpreted as a drug induced intensification of a conflict, existing in normal animals between the tendency to stay in the vicinity of the reward and the tendency to run for a subsequent reward. 14 references. (Author abstract modified)

187260 Beaton, J. M.; Smythies, J. R.; Bridgers, W. F.; McClain, L. D.; Pegram, G. V.; Bradley, R. J. Neurosciences Program, University of Alabama, University Station, Birmingham, AL 35294 **A study of the behavioral disruption of mice induced by l-methionine and related compounds.** Psychopharmcologia (Berlin). 36(2):101-108, 1974.

The behavioral disruption of mice induced by l-methionine and related compounds was studied. Mice housed in groups normally huddle together. The daily administration of 250mg/kg l-methionine induced disruption of this normal grouping behavior. Several compounds related to the metabolic pathway of methionine were also tested. The data indicate that the behavioral disruption observed was more likely due to the resultant increase in the level of one of the metabolites of methionine rather than to the increase in the number of available methyl groups. 17 references. (Author abstract)

187261 Glick, Stanley D.; Marsanico, Richard G. Beth Israel Medical Center, 307 Second Ave, New York, NY 10003 **Shifting of the d-amphetamine dose-response curve in rats with frontal cortical ablations.** Psychopharmacologia (Berlin). 36(2):109-115, 1974.

Shifting of the d-amphetamine dose response curve in rats with frontal cortical ablations is reported. Rats were trained to bar-press on a FI 15 schedule for water reinforcement and were administered various doses of amphetamine both before and 6-8 weeks after bilateral ablation of frontal cortex. Preoperatively, low doses of d-amphetamine increased responding and high doses of d-amphetamine depressed responding. Postoperatively, frontal rats showed larger facilitory effects in response to low doses of d-amphetamine; the whole dose response curve was generally shifted higher by the frontal lesions. Results indicate that frontal lesions differentially influence mechanisms mediating two different actions of d-amphetamine. 13 references. (Author abstract)

187420 Mason, S. T.; Iversen, S. D. University of Cambridge, Downing Street, Cambridge CB2 3EB, England **Learning impairment in rats after 6-hydroxydopamine-induced depletion of brain catecholamines.** Nature (London). 248(5450):697-698, 1974.

Learning impairment in rats was investigated after 6-hydroxydopamine induced depletion of brain catecholamines. On both 'trying time' and 'total time in the apparatus to solution' the 6-hydroxydopamine animals were severely impaired relative to the controls. The severe impairment in acquisition in the treated animals cannot be attributed to a motor impairment. It also seems unlikely that the deficit is motivational as the treated animals spent as much time as controls in behavior oriented toward a ball. Nor do the treated animals suffer from a retention defect. Thus, 6-hydroxydopamine treatment produced a severe impairment in the actual learning process itself. Results of a radiochemical assay of tyrosine hydroxylase confirmed that the 6-hydroxydopamine animals had sustained severe losses of adrenergic neurons in the hypothalamus, cerebral cortex and corpus striatum. 20 references.

187498 Robinson, Robert G.; Hoffer, B. J.; Bloom, F. E. St. Elizabeths Hospital, Wm. A. White Bldg., Washington, DC 20032 **Chlorpromazine induced hyperphagia. (Unpublished paper).** Washington, D. C., NIMH, 1974. 1 p.

Chlorpromazine (CPZ) induced hyperphagia was examined in rats. Over a 5 month period, 20 rats were treated with injections of either CPZ or saline. Daily food intake and weight gain were elevated in CPZ treated animals only on the first day of treatment; weight gain for the 5 mo period was less in CPZ treated animals than in controls. The 24 h activity of treated animals was decreased by 50%. This sedation was reflected in the hourly pattern of food intake, which showed that treated animals did not eat for from 6 to 10 hr after injection and then ate markedly increased amounts. The hyperphagic effect of CPZ was not due to sedation alone. It was found that treated animals ate more than controls even when required to work for food by bar pressing. (Author abstract modified)

187499 Segal, Menahem; Bloom, F. E. St. Elizabeths Hospital, Wm. A. White Bldg., Washington, DC 20032 **Effects of locus coeruleus stimulation on hippocampal unit activity and on behavior in unrestrained rats. (Unpublished paper).** Washington, DC, NIMH, 1974. 1 p.

The behavioral and neuronal effects of electrical stimulation in the nucleus locus coeruleus (LC) were studied chronically in freely moving rats. Bipolar stimulating electrodes were implanted in the LC region. First, the rat was tested for intracranial self-stimulation through the LC electrode, and the rewardability of the stimulating electrode position was assessed. Simultaneously, the responses of hippocampal cells to LC stimulation were noted. Next, the rat was trained in a classical training paradigm in which a tone was associated with milk. The effects of LC stimulation on the generation and performance of the conditioned response were assessed. The effects of adrenergic drugs were studied on self-stimulation and evoked hippocampal activity. Rats were observed to self-stimulate their LC at a high rate; cells in the hippocampus were inhibited by LC stimulation under these conditions. LC stimulation potentiates unitary conditioned responses in the hippocampus. Both self-stimulation behavior and hippocampal unit inhibitions are antagonized by alpha-methyltyrosine, and potentiated by amphetamine. (Author abstract modified)

187545 Holtzman, Stephen G.; Jewett, Robert E. Dept. of Pharmacology, Emory Univ., Atlanta, GA 30322 **Stimulation of behavior in the rat by cyclazocine: effects of naloxone.** Journal of Pharmacology and Experimental Therapeutics. 187(2):380-390, 1973.

The actions of cyclazocine, a potent analgesic with mixed agonist and narcotic antagonist properties, were evaluated on two distinct types of behavior in the rat: lever pressing maintained under a continuous avoidance schedule and locomotor activity. The effects of cyclazocine on the total brain content of norepinephrine, dopamine and serotonin were also examined. Dose response curves were determined for cyclazocine alone, then redetermined with concomitant administration of naloxone at two dose levels. d-Amphetamine was tested alone and with naloxone on avoidance behavior. Cyclazocine increased avoidance responding and locomotor activity in a graded manner over a broad range of doses. Both behaviors were disrupted by highest doses of cyclazocine. Naloxone, inactive in all procedures, attenuated the stimulant

and disruptive effects of cyclazocine on avoidance behavior but failed to block cyclazocine's effect on locomotor activity and brain catecholamine levels. Naloxone reduced the rate increasing effect of d-amphetamine on avoidance responding and enhanced the disruption of avoidance behavior produced by a high dose of the drug. 38 references. (Author abstract modified)

187551 Kellogg, Carol. Dept. of Psychology, Univ. of Rochester, Rochester, NY 14627 **Development of locomotion and brain catecholamines.** Final Report, NIMH Grant MH-23427, 1974. 3 p.

The interrelated ontogeny in the brain of certain putative transmitters is analyzed and behavioral approaches are developed to study the ontogeny of integrated motor function. Greater understanding of the contribution of neurotransmitter development to normal and abnormal motor responses in children is sought. Results indicate that there are definite periods of development of the catecholamine neurons for example where imbalances exist that can be accentuated by early L-dopa treatment and thereby pro- duce transient but noted motor deficits. It is also found that there may be periods during ontogeny where some of the suspected neurotransmitters such as serotonin are present but not located in functional neurons; their function during those periods is not understood. It is of related interest that the appearance of functional serotonin neurons corresponds to the time of marked change in the qualitative appearance of L-dopa induced locomotor activity suggesting interaction between the catecholamine and indoleamine neurones in the elaboration of this response. (Author abstract modified)

187572 Pirch, James H.; Osterholm, Karen C. Department of Pharmacology, University of Texas Medical Branch, Galveston, TX 77550 **Influence of alpha-methyltyrosine on enhancement of shuttle-box avoidance by marijuana and pentobarbital.** Research Communications in Chemical Pathology and Pharmacology. 8(2):203-211, 1974.

The influence of alpha-methyltyrosine on enhancement of shuttlebox avoidance effected in rats by marihuana and pentobarbital was investigated to determine the possible role of catecholamines in facilitating avoidance behavior. Delta9-tetrahydrocannabinol administered orally at doses of 20 or 40mg/kg enhanced shuttlebox performance of poorly performing rats, and a similar effect was produced by five or 10mg/kg of pentobarbital, given intraperitoneally. Pretreatment with alpha-methyltyrosine, 50mg/kg, antagonized the facilitative effect of marihuana but not of pentobarbital. The results indicate that the facilitative effect of marihuana on shuttlebox performance involves catecholamines, and the actions of marihuana and pentobarbital to enhance avoidance are exerted through different mechanisms. 10 references. (Author abstract modified)

187575 Nishie, K.; Norred, W. P.; Pensabene, J. W. Richard B. Russell Agricultural Research Center, ARS, USDA, Athens, GA 30604 **Effects of short-term administration of N-nitroso compounds on liver histology and pentobarbital-induced sleeping time in mice.** Research Communications in Chemical Pathology and Pharmacology. 8(2):301-311, 1974.

The effect of nitrosamines and some nitrosoureas on pentobartibal sleeping time (PST) in mice was investigated, and the ability of these compounds to produce hepatic lesions was tested. All known carcinogenic nitrosamines tested with the exception of dipentylnitrosamine, increased PST within 2 days of oral administration. Carcinogenic nitrosamines also caused loss of glycogen, lipid accumulation, swelling of hepatocytes or hemorrhage and necrosis with lymphocytic infiltration in either centrolobular or periportal areas of the liver. Dipentylnitrosamine resembled noncarcinogenic nitrosamines in causing significant reduction of PST. Dipentylnitrosamine increased the smooth endoplasmic reticulum of hepatocytes. Carcinogenic nitrosoureas did not produce visible effects in the liver histologically; but 1-butyl-1-nitrosourea, and dimethylnitrosourea increased PST; 1-methyl-1-nitrosourea and 1-ethyl-1-nitrosourea shortened PST. 13 references. (Author abstract modified)

187638 Harris, Robert T.; Waters, William; McLendon, David. Department of Physiology, Baylor College of Medicine, Houston, TX 77025 **Evaluation of reinforcing capability of delta-9-tetrahydrocannabinol in rhesus monkeys.** Psychopharmacologia (Berlin). 37(1):23-29, 1974.

The reinforcing capability of delta9-tetrahydrocannabinol (THC) was examined. Harnessed rhesus monkeys, surgically prepared with indwelling jugular catheters, were given access by means of remotely controlled infusion pumps to unlimited quantitites of delta9-trans-tetrahydrocannabinol. Naive monkeys as well as monkeys which were automatically infused with THC for over 28 days did not self-administer THC. Monkeys which had a history of multiple drug self-administration also did not self-infuse THC. 9 references. (Author abstract).

187640 Jones, Byron C.; Clark, Dennis L.; Consroe, Paul F.; Smith, Harriet J. Dept. of Pharmacology and Toxicology, College of Pharmacy, Uiversity of Arizona, Tucson, AZ 85721 **Effects of (-) delta9-trans-tetrahydrocannabinol on social behavior of squirrel monkey dyads in a water competition situation.** Psychopharmacologia (Berlin). 37(1):37-43, 1974.

Delta9-THC induced changes in competitive and noncompetitive social behaviors, activity and incentive motivation in squirrel monkeys were studied. Delta9-THC in doses of 0.25, 0.5or 1.0mg/kg was administered to pairs of squirrel monkeys in a water competition test. After stable baseline measures for the pairs were obtained, repeated testing of pairs followed the sequence of orally treating the dominant member, the submissive member, and both members of the pairs. Total competition behaviors decreased when both members received 1 mg/kg, but increased when either the submissive member or both members of low competitive pairs received 0.25 mg/kg. Noncompetitive social behaviors increased when both animals were drugged, an effect which was maximal at 1.0mg/kg. Delta9-THC produced the most salient effects when both animals were drugged and demonstrated a biphasic dose effect on competition. 9 references. (Author abstract).

187641 Van der Poel, A. M. Dept. of Fundamental Pharmacology, University of Leiden, Wassenaarseweg 62, Leiden, The Netherlands **The effect of some cholinolytic drugs on a number of behavioural parameters measured in the T-maze alternation test: dose-response relationships.** Psychopharmacologia (Berlin). 37(1):45-58, 1974.

The relationships between dose and the various response measured in the T-maze alternation test were compared. Conflict behavior in a T-maze can be observed at the choice point, involving simultaneous tendencies to move left and right and in the goal box involving simultaneous tendencies to approach the reward and to return towards the choice point. Firstly, the effects of different doses (from 0.06 to 1 mg/kg) of the cholinolytic drug 3-quinuclidinyl benzilate on the alternation of choice directions and on the choice point conflict were studied. Secondly, the goal box conflict was studied following ad-

ministration of different doses (0.03 to 1 mg/kg) of another cholinolytic drug N-methyl-4-piperidyl methylethynyl-glycolate. It was observed that the suppression of alternation to chance levels developed at similar dose levels as the intensification of the conflict behavior. The present observations are in agreement with a previous dose response study of 3-quinuclidinyl benzillate and behavioral conflict in a circular runway. 25 references. (Author abstract).

187666 Broekkamp, C. L. E.; van Rossum, J. M. Dept. of Pharmacology, Geert Grooteplein 21 Noord, Nijmegan, The Netherlands **Effects of apomorphine on self-stimulation behavior.** Psychopharmacologia (Berlin). 34(1):71-80, 1974.

Self-stimulation behavior was studied in untreated rats and rats injected with apomorphine with electrodes implanted in the nucleus accumbens, the lateral hypothalamus, the catecholaminergic cell groups A9 - A10 and the locus coeruleus. Apomorphine (0.2mg/kg s.c.)consistently facilitated self-stimulation in a number of rats but inhibited this behavior in others. This individual variation could be observed in all four groups of rats but was further analysed in the rats with an electrode in the A9 - A10 area. The effect of the drug was highly reproducible for individual animals. Extinction after reduction of the rewarding current to zero could not be demonstrated as long as the drug was active. These results substantiate the hypothesis that apomorphine is able to replace the reinforcing action of intracranial rewarding stimulation. (Author abstract)

187696 Howard, James L.; Grant, Lester D.; Breese, George R. Biological Sciences Research Center, Child Development Institute, School of Medicine, Univ. of North Carolina, Chapel Hill, NC 27514 **Effects of intracisternal 6-hydroxydopamine treatment on acquisition and performance of rats in a double T-maze.** Journal of Comparative & Physiological Psychology. 86(6):995-1007, 1974.

The effects of intracisternal 6-hydroxydopamine on acquisition and performance of rats were studied. Male rats were subjected to various treatments with 6-hydroxydopamine (6-OHDA) to produce decrements in brain catecholamine content either before or after learning to respond to an appetitively motivated double T-maze. Intracisternal injections of 6-OHDA not only impaired acquisition of the required behavioral response but also decreased performance of animals which had previously acquired the task. Although decreased food consumption found in 6-OHDA treated animals may contribute to the observed deficits in T-maze responding, the behavioral deficit produced by 6-OHDA injection did not seem to be due only to a simple decrease in food intake. The decrements in acquisition and performance were clearly related to amount of central catecholamine depletion produced by 6-OHDA treatment. It is suggested that behavioral deficits are more related to reductions in dopamine than to the depletion of brain norepinephrine. 33 references. (Author abstract modified)

187697 King, Alan R.; de Wied, David. Psychology Teaching Group, Plymouth Polytechnic, Plymouth PL4 8AA, Devon, England **Localized behavioral effects of vasopressin on maintenance of an active avoidance response in rats.** Journal of Comparative & Physiological Psychology. 86(6):1008-1018, 1974.

The role of lysine vasopressin (LVP) in maintaining shock avoidance behavior under extinction conditions was investigated; a pole jump situation was used. In three experiments, a single injection of LVP was administered to rats on the first acquisition session. The following results were obtained: resistance to extinction occurred when LVP effects were restricted to a single correct response; similar effects occurred when the injection was delayed until immediately after the trial; classical conditioning alone was a sufficient behavioral substrate for the effects but instrumental conditioning was more effective. In the fourth experiment, LVP produced increased resistance to extinction when given in association with behavior which accelerated extinction. 12 references. (Author abstract)

187698 Neill, Darryl B.; Boggan, William O.; Grossman, Sebastian P. Emory Univ., Atlanta, GA **Behavioral effects of amphetamine in rats with lesions in the corpus striatum.** Journal of Comparative & Physiological Psychology. 86(6):1019-1030, 1974.

The behavioral effects of amphetamine were examined in rats with lesions of the corpus striatum. Lesions in the ventral striatum of rats lowered forebrain dopamine and impaired avoidance behavior more severely than comparable lesions in the dorsal striatum. Ventral striatal damage also antagonized the effects of d,l-amphetamine on stereotyped behavior and on intertrial activity. Lesions in the dorsal striatum did not modify the effect of amphetamine in these tests. Neither the dorsal nor the ventral striatal lesions significantly depleted forebrain norepinephrine and both failed to affect the facilitatory effects of amphetamine on exploratory activity in an open field. The hypothesis that some but not all of the behavioral effects of amphetamine may be due to the drug's action on dopaminergic components of the striatum is supported. 32 references. (Author abstract)

187699 Heffner, Thomas G.; Drawbaugh, Richard B.; Zigmond, Michael J. Dept. of Biology, Univ. of Pittsburgh, Pittsburgh, PA 15260 **Amphetamine and operant behavior in rats: relationship between drug effect and control response rate.** Journal of Comparative & Physiological Psychology. 86(6):1031-1043, 1974.

The effect of amphetamine on the rate of operant responding was examined using rats trained to press a lever for water reinforcement. Amphetamine's effect was strongly correlated with mean predrug rate of responding. Drug induced increases in rate were inversely proportional to control rates, while drug induced decreases were directly proportional to control rates. This relationship was observed in different groups of rats trained to perform on different types of reinforcement schedules (fixed-ratio, fixed-interval and variable interval), in a single group of rats performing on different schedules of the same type (different fixed-ratios) and for a single group of rats performing in different segments of the same schedule (fixed-interval). 36 references. (Author abstract)

187700 Schwartzbaum, J. S.; Ide-Johanson, L.; Belgrade, J. Dept. of Psychology, Univ. of Rochester, Rochester, NY 14627 **Comparative effects of scopolamine and amphetamine upon behavioral reactivity and visual evoked potentials to flashes in rats.** Journal of Comparative & Physiological Psychology. 86(6):1044-1051, 1974.

Averaged visual evoked response (VER) at cortex and behavioral reactivity to photic stimuli were examined in the rat following administration of varying dosages of either scopolamine (and methyl scopolamine) or d-amphetamine and of saline. The augmentation in behavioral activity produced by scopolamine and d-amphetamine was associated with differential patterns of changes in VERs. Scopolamine reduced the amplitude of the early negative component, enhanced the early positive component and blocked the attenuation of the late negative wave normally associated with heightened

behavioral activity. Amphetamine produced relatively selective decrements in the late negative wave which at higher dosages related to flash sequence. 18 references. (Author abstract modified)

187701 Dennis, Stephen G. Dept. of Psychology, Univ. of California, San Diego, La Jolla, CA 92038 **Temporal aspects of scopolamine-induced one-way memory dissociation in mice.** Journal of Comparative & Physiological Psychology. 86(6):1052-1058, 1974.

The temporal aspects of scopolamine induced one way memory dissociation were studied in mice. Mice were trained in a single session on an object discrimination shock - escape task after an injection of scopolamine or saline. They were subsequently required to relearn the task after 1, 2, or 4 days with half the animals receiving the same agent as on training, the other half receiving the opposite agent. Results from the 2 day experiment support a dual effect model of one way dissociation which postulates two actions of the drug: a reduction in learning efficiency; and scopolamine state dependency. The pattern of results of the 1 day experiment shows a much attenuated state dependency effect while the 4 day groups showed no significant intergroup differences, violating both postulates. It is suggested that one way memory dissociation and specifically the concept of state dependency, be reconsidered in terms of the temporal aspects of the memory process. 21 references. (Author abstract modified)

187702 Satinder, K. Paul; Petryshyn, W. Roman. Dept. of Psychology, Lakehead Univ., Thunder Bay, Ontario, Canada P7B 5E1 **Interaction among genotype, unconditioned stimulus, d-amphetamine, and one-way avoidance behavior of rats.** Journal of Comparative & Physiological Psychology. 86(6):1059-1073, 1974.

In the genetic analysis of avoidance learning, questions relating to the generality to other avoidance behaviors and the role of motivation were investigated in two strains of rats. Significant differences were found in one way avoidance behavior of the strains selectively bred for two way active avoidance. In six experiments reported, these differences in one way avoidance either disappeared or were minimized to a great extent under the effects of d-amphetamine. The experimental manipulation of motivation, unconditioned stimulus shock level equivalent to the unconditioned flinch, jump and fleeing response measures accounted for only part of the variation in avoidance learning of these strains. Results are discussed in terms of inverted-U arousal function and quantitative genetics. 19 references. (Author abstract)

187703 Plotnik, Rod; Mollenauer, Sandra; Snyder, Elaine. Department of Psychology, San Diego State Univ., San Diego, CA 92115 **Fear reduction in the rat following central cholinergic blockade.** Journal of Comparative & Physiological Psychology. 86(6):1074-1082, 1974.

Fear reduction in the rat was studied following central cholinergic blockade. In the presence of cats, rats showed a constellation of responses that were used to define fear: freezing, avoiding the cat and suppressing consumatory behavior. Compared with controls, rats treated with an anticholinergic drug, scopolamine, showed less freezing and significantly more approach of the cat and actually engaged in consumatory behavior in proximity to the cat. On a second, undrugged exposure to the cat, the original scopolamine treated animals continued to show significantly less freezing, more approach and more drinking than controls. Since methyl scopolamine, which mimics the peripheral actions of scopolamine, had no effect on fear responses, these results implicate a central cholinergic system in fear responses of species typical defense reactions. 24 references. (Author abstract modified)

187868 Angel, Charles; Murphree, Oddist D.; DeLuca, Donald C. europsychiatric Research, Veterans Administration Hospital, North Little N Rock, AR 72114 **The effects of chlordiazepoxide, amphetamine and cocaine on bar-press behavior in normal and genetically nervous dogs.** Diseases of the Nervous System. 35(5):220-223, 1974.

The effects of chlordiazepoxide, amphetamine and cocaine on bar-press behavior in normal and genetically nervous dogs were examined. Studies on two strains of pointer dogs have demonstrated that administration of a benzodiazepine, chlordiazepoxide, facilitates acquisition of goal directed behavior in genetically nervous subjects. Continued administration of the drug is required to maintain bar-press response in this strain. The concomitant administration of either cocaine or amphetamine, compounds which inhibit neuronal reuptake of norepinephrine, disrupts the behavioral response of the genetically nervous E-strain subjects to a far greater extent than the stable A-strain subjects. It was shown that after 14 days of daily administration of chlordiazepoxide, withdrawal of the drug not only resulted in almost complete loss of bar-press response in the E-strain subjects, but also resulted in a temporary decrease in the acquired behavioral response of the stable A-strain subjects. 11 references. (Author abstract modified)

187925 Goudie, A. J.; Taylor, Max. Department of Psychology, University College of North Wales, Bangor, Caernarvonshire, North Wales **Time sampling of rat exploratory behaviour: a reliable screening test for the C.N.S. effects of anorexic agents.** Psychopharmacologia (Berlin). 35(1):1-12, 1974.

A series of eight experiments was conducted on the acute effects of several anorexic agents of rat exploratory behavior, as assessed by a time sampling procedure of behavioral categorization. Compounds studied included some anorexiants, fenfluramine derivatives, and an indole derivative. The results indicate that amphetamine and diethylpropion are stimulants while fenfluramine is a sedative. The technique of activity analysis described is a useful screening test for psychotropic agents which affect central nervous system excitability in humans, but it is noted that the effects of acute administration do not always provide a reliable index of chronic effects. 50 references. (Author abstract modified)

187926 Taylor, Max; Goudie, A. J. Department of Psychology, University College of North Wales, Bangor, Caernarvonshire, North Wales **Chronic anorexic and behavioural effects of the fenfluramine derivative SE 780 in rats.** Psychopharmacologia (Berlin). 35(1):13-17, 1974.

The behavioral and anorexic effects of the fenfluramine derivative SE 780 in rats were studied after chronic administration over 35 days. Behavioral effects of the compound were assessed by time sampling behavioral categorization, on days 1, 14, and 28 of administration. An initial sedative effect observed after acute administration was absent on days 14 and 28, when the drug had no behavioral effects at all. The anorexic properties of the drug were investigated by measuring daily bodyweights and intake of food over a 2 h period on observation days. The drug appeared to be a highly potent anorexiant which may be superior to fenfluramine by lacking stimulant properties after chronic administration and by being active over longer periods of time. Its study in humans is advocated. 7 references. (Author abstract modified)

187930 Tilson, H. A.; Rech, R. H. Bristol Laboratories, Pharmacology Research, Syracuse, NY 13201 **The effects of p-chlorophenylalanine on morphine analgesia, tolerance and dependence development in two strains of rats.** Psychopharmacologia (Berlin). 35(1):45-59, 1974.

The effects of p-chlorophenylalanine (p-CPA) on morphine analgesia and the development of tolerance and physical dependence were investigated in Sprague Dawley (SD) and Fisher (F) strains of albino rats. F strain rats were more reactive to electric footshock than SD rats, but showed less relative increase in threshold (analgesia) than SD rats following various doses of morphine. Pretreatment with p-CPA attenuated significantly morphine analgesia in SD, but not F rats. Assuming difference in the function of the serotonergic inhibitory system in the two strains of rats, the data provide general support for the involvement of brain 5-HT mechanisms in modulating if not mediating the effects of morphine. 32 references. (Author abstract modified)

187932 Huang, Jen-Tzaw; Ho, Beng T. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **The effect of pretreatment with iproniazid on the behavioral activities of beta-phenylethylamine in rats.** Psychopharmacologia (Berlin). 35(1):77-81, 1974.

Rats were trained on DRL 15 sec schedule to choose between two response levers in the operant chamber in order to obtain a food pellet, with the choice of lever depending upon intraperitoneal injection of d-amphetamine sulfate or saline as the cue for response. Beta-phenylethylamine HCl or iproniazid phosphate alone did not produce the discriminative cue similar to d-amphetamine. With treatment of animals with iproniazid prior to the administration of beta-phenylethylamine to prevent the metabolism of the latter, the discriminative cue similar to d-amphetamine can then be generated by beta-phenylethylamine. Iproniazid caused decreased spontaneous locomotor activity in rats while beta-phenylethylamine did not affect this behavior. It is suggested that the amphetamine like increase in motor activity produced by beta-phenylethylamine was masked by iproniazid which was shown to decrease spontaneous locomotor activity. 7 references. (Author abstract modified)

188166 Urban, I.; Lopes da Silva, F. H.; van Leeuwen, W. Storm; De Wied, D. Rudolf Magnus Institute for Pharmacology, University of Utrecht, Utrecht, Holland **A frequency shift in the hippocampal theta activity: an electrical correlate of central action of ACTH analogues in the dog?** Brain Research (Amsterdam). 69(2):361-365, 1974.

The influence of adrenocorticotropic hormone (ACTH) in position 7 (ACTH4-10(7-L-phe)) and ACTH(7-D-phe) on electrical activity of the brain was studied in a freely moving dog in an operant conditioning situation, using chronically indwelling electrodes and a radio telemetering technique. The 10 month study consisted of three experimental periods in which two food deprivation schedules (mild and strong) were used. Findings indicate that the pattern of hippocampal electrical activity during 'facing' periods is quite stable, reproducible and typical for comparable experimental conditions. This parameter is also sensitive to changes in food deprivation levels resulting in an increased stability of performance when the level of deprivation increases. Both analogs modified the typical pattern of hippocampus activity only under mild deprivation levels. Results indicate that the central nervous system of the dog is sensitive to the two ACTH analogs devoid of corticotrophic activities which have been shown to modify conditioned behavior in rats in the opposite manner. 10 references.

188248 Kurtz, Perry; Palfai, Tibor. Collendale Psychology Labs, B-7 Colvin Lane, Syracuse University, Syracuse, NY 13210 **Behavioral and electrocorticographic dose-response relationships with Metrazol. (Unpublished paper).** Syracuse, Syracuse Univ., 1972, 5 p.

Behavioral and electrocorticographic dose - response relationships with Metrazol were examined in three experiments. Experiment one investigated the possibility that subconvulsive doses of Metrazol can produce state dependent learning. Experiment two examined the effect of lowered Metrazol doses on reversal attention. Subjects were mice 10 to 12 weeks old. Data from experiment one suggest that a subconvulsive dose of Metrazol produces asymmetrical dissociation. Results from experiment two suggest that facilitation of reversal retention may have occurred. A third experiment studying the effects of Metrazol dosages on electrocorticogram is described.

188251 no author. no address **The effects of pentylene-tetrazol (Metrazol) on a learned taste aversion produced by lithium chloride: the issue of associative memory vs. retentive memory. (Unpublished paper).** Research Report, NIMH Grant MH-23225, 1974, 4 p.

The effects of pentylene-tetrazol (Metrazol) on a learned taste aversion produced by lithium chloride are discussed. Metrazol was administered to rats under two conditions: 1) after the CS-UCS pairing, so that the UCS trace could be disrupted, but minimal concurrent interference with association would occur; 2) between the CS-USC pairing, so that although the CS trace could be disrupted, maximal concurrent association could occur. The administration of Metrazol under the first condition did not result in decreased suppression. Under the second condition, Metrazol interfered with the association of the CS with the UCS. In this instance Metrazol produced associative interference but no amnesia.

188412 Millner, Judith R.; Palfai, Tibor. Department of Psychology, Syracuse University, Syracuse, NY 13210 **Metrasol disrupts conditioned aversion produced by LiCl: a time dependent effect.** Research Report, NIMH Grant MH-23225, 1974. 10 p.

The effects of Metrazol induced seizures on a conditioned saccharin aversion produced by LiCl were studied in two experiments with rats. Findings of the first experiment indicate that Metrazol administered 10 minutes before or after LiCl does not interfere with the retention of a conditioned aversion to saccharin. In the second experiment, Metrazol was given within 5 seconds after the administration of LiCl; under these conditions, impairment occurs. It is concluded that Metrazol may interfere with the retention of a conditioned taste aversion in a time dependent manner. 8 references. (Author abstract modified)

188605 Squire, Larry R.; Barondes, Samuel H. Department of Psychiatry, University of California, San Diego, La Jolla, CA 92037 **Anisomycin, like other inhibitors of cerebral protein synthesis, impairs 'long-term' memory of a discrimination task.** Brain Research (Amsterdam). 66(2):301-308, 1974.

The role of anisomycin in the impairment of long-term memory of a discrimination task was examined in mice. Anisomycin, an inhibitor of cerebral protein synthesis, impaired memory measured 1, 7, or 14 days after training. Concurrent tests with cycloheximide indicated that the two drugs exerted identical effects on memory. Like cycloheximide, anisomycin had no effect on acquisition with brief training but impaired performance of mice during prolonged training. Anisomycin

depressed spontaneous locomotor activity, but an analog which shared this activity effect inhibited cerebral protein synthesis far less and had no amnesic effect. Anisomycin represents a third class of protein synthesis inhibitor, in addition to puromycin and cycloheximide, which impairs long-term memory after discrimination training. These results considerably strengthen the contention that cerebral protein synthesis is required for long-term memory. 23 references. (Author abstract)

188611 Eliasson, Mona. Department of Medical Pharmacology, University of Uppsala, Biomedical Center, Uppsala, Sweden **Effects of LSD and monoamine synthesis inhibitors on hormone-activated copulatory behavior in the female rat.** Brain Research (Amsterdam). 66(2):369, 1974.

At the fifth annual meeting of the European Brain and Behavior Society, effects of lyseric acid diethylamide (LSD) and monoamine synthesis inhibitors on hormone activated copulatory behavior in the female rat were reported. LSD had a very clear inhibitory effect on the lordosis response, as would be predicted from previous studies. Concomitantly with this inhibition the animals also showed a hyperreactivity to sudden stimuli together with vocalization when touched by the experimenter or the test male. When the subjects had been pretreated 5 h before LSD with p-chlorophenylalanine (PCPA) which inhibits the synthesis of serotonin primarily, the inhibition of the lordosis was significantly prolonged. The inhibition was still present several hours after animals treated with LSD alone had recovered a normal level of responding. Pretreatment 5 h before LSD with alpha-methyl-p-tyrosine, a blocker of catecholamine synthesis, on the other hand, attenuated the LSD effect significantly and shortened its duration, despite a rather heavy sedation after this treatment combination. The results suggest that decreased serotonin biosynthesis would facilitate the agonistic effect of LSD on hormone activated lordotic behavior in ovariectomized female rats. (Author abstract modified)

188620 Robbins, Trevor; Iversen, Susan D. Department of Experimental Psychology, University of Cambridge, Cambridge, England **An investigation of the behavioural nature of the psychomotor stimulant effect of amphetamine.** Brain Research (Amsterdam). 66(2):363, 1974.

At the fifth annual meeting of the European Brain and Behavior Society, the behavioral nature of the psychomotor stimulant effect of amphetamine was examined in the rat. A modified Berlyne box was used to obtain independent measures of locomotor activity and exploration of novel stimuli in the same situation. D-Amphetamine was found to stimulate locomotor activity and decrease exploratory behavior when compared with a control group. These behaviors were found to be compatible in undrugged animals when distributed over the 10 min trial. The results are discussed in terms of an indirect inhibition of exploratory behavior by drug induced response incompatibility rather than by direct inhibition of such behavior. In a second experiment, a signal detection analysis of the effect of the drug on temporal discrimination in rats revealed that with low doses of the drug there were significant changes in response bias, reflected as an overall tendency to respond, unaccompanied by changes in sensitivity to temporal cues. It is implied that the drug induced disruption of the discrimination arises as an indirect result of this tendency, rather than as a direct inhibition of temporal discrimination. (Author abstract)

188637 Stokes, John D.; Scudder, Charles L. Department of Pharmacology, Stritch School of Medicine, Loyola University, 2160 South First Avenue, Maywood, IL 60153 **The effect of butylated hydroxyanisole and butylated hydroxytoluene on behavioral development of mice.** Developmental Psychobiology. 7(4):343-350, 1974.

The chronic ingestion of .5% butylated hydroxyanisole (BHA) or butylated hydroxytoluene (BHT) by pregnant mice and their offspring resulted in a variety of behavioral changes. Compared to controls, BHA treated offspring showed increased exploration, decreased sleeping, decreased self-grooming, slower learning, and a decreased orientation reflex. BHT treated offspring showed decreased sleeping, increased social and isolation induced aggression, and a severe deficit in learning. 22 references. (Author abstract)

188760 Black, W. C.; Grosz, H. J. Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46202 **Propranolol antagonism of morphine-influenced behavior.** Brain Research (Amsterdam). 65(2):362-367, 1974.

Propranolol antagonism of morphine influenced behavior was studied in the rat. Findings showed that pretreatment with Inderal (the racemic mixture) attenuated morphine produced alleviation of behavioral suppression. Dextro-propranolol manifested inconsistent but reliable interaction with morphine. Pretreatment with the dextro isomer greatly reduced the disruption of avoidance behavior by morphine; Inderal, l-propranolol, or saline failed to reduce this response. Morphine increased the number of shocks received without reducing the number of responses. It is concluded that dextro-propranolol might protect against the degradation of preshock behavior and may retard the increase in postshock behavior while the l-isomer and the racemic mixture fail to have these effects on morphine produced alterations in behavior. 16 references.

189025 Franklin, K. B. J.; Herberg, L. J. Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG, England **Self-stimulation and catecholamines: drug-induced mobilization of the 'reserve'-pool re-establishes responding in catecholamine-depleted rats.** Brain Research (Amsterdam). 67(3):429-437, 1974.

Electrical self-stimulation and catecholamines were studied to determine if drug induced mobilization of the reserve pool reestablished responding in the catecholamine depleted rats. Suppression of electrical self-stimulation by the catecholamine (CA) synthesis blocker alpha-methyl-p-tyrosine (alpha-MPT) has been taken to mean that the reinforcement process depends critically on the availability of freshly synthesized CA stored in a small functional intraneuronal pool. But more recently a temporary recovery of responding was observed after short rest periods, and this recovery has been attributed to the availability of CA mobilized from the reserve pool. Findings are reported which support the latter theory. A stimulant phenylethylamine derivative (methylphenidate) facilitating mobilization of the reserve pool produced an immediate, pronounced and long-lasting restoration of self-stimulation after its suppression by alpha-MPT, but not if the reserve pool were first dispersed by the administration of reserpine. 16 references. (Author abstract modified)

189215 Schmaltz, Gerard; Delerm, Bernard. Laboratoire de Psychophysiologie, Universite de Lille I, BP 36 59650 Villeneuve d'Ascq, France **/Effects of cycloheximide on acquisition and retention of avoidance learning in the rat: recovery of memory./** Effets du cycloheximide sur la memorisation d'un

apprentissage d'evitement chez le rat: recuperation mnesique. Physiology & Behavior. 13(2):211-220, 1974.

The effects of cycloheximide on acquisition and retention of an avoidance learning in the rat were studied. Thirty minutes before an avoidance learning session in a Y maze, rats were given a subcutaneous injection of either cycloheximide or saline. The results show acquisition is not affected by the severe protein synthesis inhibition. Impairment of memory is found only in the low criterion experimental group 2 hr after learning and in both experimental groups 24 hr after learning. A recovery of memory was observed in both groups 6 days later. A control experiment indicates that the deficits found cannot be regarded as retrieval deficits. Transient amnesia is interpreted in terms of slowing down in long-term memory establishment process and this is thought to be due to a decrease in the rate of neurotransmitter synthesis. 37 references. (Author abstract modified)

189399 Yehuda, Shlomo; Wurtman, Richard J. Department of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Paradoxical effects of d-amphetamine on behavioral thermoregulation: possible mediation by brain dopamine.** Journal of Pharmacology and Experimental Therapeutics. 190(1):118-122, 1974.

The paradoxical effects of d-amphetamine on behavioral thermoregulation were studied in rats. Doses of d-amphetamine which produce hypothermia or hyperthermia at low or high ambient temperature also interfere with the ability of the rats to utilize behavior as a mechanism for thermoregulation. Rats given d-amphetamine and placed in a cold environment choose not to locate themselves beneath a heat lamp, even though body temperature falls; control rats, whose normal body temperature is maintained, elect to position themselves near the heat lamp. Conversely, hyperthermic d-amphetamine treated rats placed in a warm environment choose paradoxically to locate themselves beneath the heat lamp; control animals do not. Drugs that interfere with the interaction between dopamine and its postsynaptic receptors block the induction of paradoxical thermoregulatory behavior by d-amphetamine, while dopaminergic agonists mimic the effect of d-amphetamine. 14 references. (Author abstract)

189405 Ferraro, Douglas Peter; Grilly, David M. Department of Psychology, University of New Mexico, Albuquerque, NM 87131 **Effects of chronic exposure to delta9-tetrahydrocannabinol on delayed matching-to-sample in chimpanzees.** Psychopharmacologia (Berlin). 37(2):127-138, 1974.

The effects of chronic exposure to delta9-tetrahydrocannabinol (THC) on delayed matching to sample were studied in chimpanzees. The initial administrations of the drug before but not after each matching to sample session produced a significant decrease in accuracy. During the course of the chronic drug regimen, animals in the experimental group recovered very slowly from this initial impairment in matching to sample performance. The extent to which the experimental animals recovered seemed to depend upon their preexperimental drug histories. The drug experienced animals developed complete tolerance within 5 weeks while the previously drug naive animals did not do so even after 5 months exposure to the drug. No residual or long-term effects were observed following termination of the chronic drug regimen. 22 references. (Author abstract modified)

189409 Dantzer, R.; Baldwin, B. A. INRA, Station de Pharmacologie, 180, chemin de Tournefeuille, F-31300 Toulouse, France **Effects of chlordiazepoxide on heart rate and behavioural suppression in pigs subjected to operant conditioning procedures.** Psychopharmacologia (Berlin). 37(2):169-177, 1974.

The effects of chlordiazepoxide on heartrate and behavioral suppression were studied in pigs subjected to operant conditioning procedures. Two groups of four pigs were subjected to a punishment discrimination (conflict) or to a nonreinforcement procedure. Conflict behavior was evidenced by the suppression of operant responding and the occurrence of a marked decrease in heartrate during the presentation of the conditioned stimulus. Pigs in the nonreinforcement procedure showed no consistent changes in heartrate although an important decrease occurred in response rate. Chlordiazepoxide was administered in order to establish whether it would attenuate the response suppression in either procedure. The drug produced a weak attenuation of conflict in terms of the operant and heartrate responses at the maximum dose used and a small disinhibiting effect on the nonreinforced responding at 10mg/kg. 16 references. (Author abstract)

189514 File, Sandra E.; Pope, J. H. Psychology Department, City of London Polytechnic, Central House, Whitechapel High Street, London E1 7 PF, England **The action of chlorpromazine on exploration in pairs of rats.** Psychopharmacologia (Berlin). 37(3):249-254, 1974.

The action of chlorpromazine on exploration was examined in pairs of rats. When two animals were placed in a hole board the number of head dips made by each rat was twice the number made when tested alone, but was the same for pairs of chlorpromazine drugged and undrugged rats, and for pairs where only one rat was drugged. This contrasts with the reduction of head dipping produced by chlorpromazine in single animals. Chlorpromazine still reduced general motor activity, regardless of whether the partner was drugged or not. The activity of the undrugged rats was affected by the partner's state and was lower when the partner was drugged. 11 references. (Author abstract)

189515 Cooper, Barrett R.; Cott, Jerry M.; Breese, George R. 226 Biological Research Center, University of North Carolina, School of Medicine, Chapel Hill, NC 27514 **Effects of catecholamine-depleting drugs and amphetamine on self-stimulation of brain following various 6-hydroxydopamine treatments.** Psychopharmacologia (Berlin). 37(3):235-248, 1974.

Changes in electrical self-stimulation responding were examined in rats with electrodes implanted in the lateral hypothalamus following 6-hydroxydopamine treatments which depleted brain dopamine, norepinephrine or both of these catecholamines. Acute depression of self-stimulation occurred after treatments which reduced brain dopamine, but did not occur in rats treated to deplete just brain norepinephrine. A chronic deficit in self-stimulation responding occurred in rats treated with 6-hydroxydropamine in combination with pargyline to reduce both brain amines, while responding of animals in which brain dopamine was reduced returned to levels observed prior to 6-hydroxydopamine treatment. Administration of the dopamine-beta-hydroxylase inhibitor, U-14624, failed to affect self-stimulation in spite of an additional 70% reduction of brain norepinephrine content. Results support the hypothesis that central dopaminergic fibers have an important involvement in the maintenance of self-stimulation of brain. 39 references. (Author abstract modified)

189516 Stadnicki, Stanley W.; Schaeppi, Ulrich; Rosenkrantz, Harris; Braude, Monique C. Mason Research Institute, 23 Harvard St., Worcester, MA 01608 **Crude marihuana extract: EEG and behavioral effects of chronic oral administration in**

rhesus monkeys. Psychopharmacologia (Berlin). 37(3): 225-233, 1974.

The toxic effects of chronic oral treatment with crude marihuana extract upon elecroencephalogram (EEG) and behavior of Rhesus monkeys were examined. Three Rhesus monkeys were treated daily po with crude marihuana extract (CME) containing delta 9-tetrahydrocannabinol (THC) 22-25% cannabidiol 2-3% and cannabinol 2-3%. CME with the equivalent of THC or more caused sedation, ptosis, ataxia, huddled posture, spontaneous jerky body movements and increased EEG synchrony without an initial phase of increased motor activity. THC produced specific EEG changes including the appearance of protracted trains of 20-25 cps rhythmic activity in thalamus and cerebellar nuclei. THC caused 1.5-2 cps slow waves in hippocampus, amygdala and septum. EEG manifestations after oral treatment were therefore different from those previously observed following i.v. injection or smoke inhalation. Behavioral effects consistently preceded and outlasted EEG changes, and tolerance developed more rapidly to specific EEG changes than to behavioral effects. 17 references. (Author abstract modified)

189519 Beaton, J. M.; LeBlanc, A. E.; Webster, C. D. Department of Psychiatry, University of Alabama, Birmingham, AL 35294 **The effects of d-amphetamine on the inter-response times of rats and guinea-pigs on a modified Sidman discriminated avoidance schedule.** Psychopharmacologia (Berlin). 37(3):199-203, 1974.

The effects of d-amphetamine on the interresponse times of rats and guinea pigs on a modified Sidman discriminated avoidance schedule were examined. Four rats and four guinea pigs were trained under a modified Sidman discriminated bar press avoidance schedule. The guinea pigs acquired the avoidance response more rapidly than the rats. The Bovet-Gatti d-amphetamine profiles were similar in both species in that there was a significant increase in responding before the stimulus light and click were presented and the interresponse times of efficient responses were shorter. The data indicated that guinea pigs may be better subjects for psychopharmacological work involving discriminated bar press avoidance behavior. 13 references. (Author abstract)

189521 Barrett, Robert J.; Leith, Nancy J.; Ray, Oakley S. Veterans Administration Hospital, 1310 24th Ave. South, Nashville, TN 37203 **An analysis of the facilitation of avoidance acquisition by d-amphetamine and scopolamine.** Behavioral Biology. 11(2):189-203, 1974.

The facilitation of avoidance acquisition produced by d-amphetamine and scopolamine was analyzed in rats. Albino rats from an inbred strain (F344s) and a random bred Sprague-Dawley derivative (ZMs) were administered intraperitoneal injections of either saline, d-amphetamine, scopolamine, or a combination of both drugs 30 min prior to daily sessions of 25 trials on a brightness discrimination, active avoidance task in completely automated Y-mazes. All drug treatments significantly facilitated acquisition of the avoidance response. This facilitation was due to increase in active responses which provided a behavioral baseline which was compatible with learning the requirements of the task. The major effect of the drugs on the F344s, who normally avoid well, was a disruption of behavior in the combination group, indicating the importance of assessing the behavioral baseline which exists prior to drug administration. 24 references. (Author abstract modified)

189525 Miczek, Klaus A.; Barry, Herbert, III. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Delta9-tetrahydrocannabinol and aggressive behavior in rats.** Behavioral Biology. 11(2):261-267, 1974.

The interaction effect of delta9-tetrahydrocannabinol on aggressive behavior was examined in rats. Fighting by pairs of albino rats, in a situation without painful shock, was measured by frequency or duration of dominant behaviors (biting attacks, threat postures, allogrooming, autogrooming), defensive - submissive behaviors (defensive - upright, submissive - supine and immobile - crouching postures), and mutual upright postures. Administration of tetrahydrocannabinol to the subordinate rat impaired the defensive - submissive behaviors, while the nondrugged dominant rat's biting attacks became more frequent and injurious. Administration of the drug to the dominant rat greatly reduced attacks and threats toward the nondrugged subordinate rat, and the dominance was weakened but not reversed. 18 references. (Author abstract)

189573 Fernandes, M.; Kluwe, S.; Coper, H. Institut fur Neuropsychopharmakologie der Freien Universitat Berlin, D-1000 Berlin 19, Ulmenallee 30, Germany **Cannabinoids and hexobarbital induced loss of righting reflexes.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(4):431-435, 1974.

The influence of cannabinoids on hexobarbital sleeping time, blood and brain levels and on the metabolism of hexobarbital in vitro by rat liver microsomes was investigated. Cannabidiol (CBD) prolongs the hexobarbitone induced loss of righting reflexes stronger than delta9 tetrahydrocannabinol (THC). The effects of CBD can be explained by an inhibition of the hexobarbital metabolism. It prolongs the half-life of the barbiturate in the blood, does not affect the hexobarbital awakening levels in the brain and inhibits strongly the degradation by liver microsomes. The THC effect, however, is predominantly produced by an interaction in the CNS. THC did not affect the hexobarbital blood levels and was much weaker in inhibiting its degradation in vitro. The awakening levels of the barbiturate in the brain, however, were significantly lowered. 16 references. (Author abstract)

189613 Abdallah, Abdulmuniem H.; White, Harold D.; Kulkarni, Anant S. Chemical Biology Research, Dow Chemical Company, Midland, MI 48640 **Interaction of d-amphetamine with central nervous system depressants on food intake and spontaneous motor activity of mice.** European Journal of Pharmacology (Amsterdam). 26(1):119-121, 1974.

The interactions of d-amphetamine with central nervous system depressants on food intake and spontaneous motor activity of mice were studied. Pentobarbital, chlordiazepoxide, diazepam, meprobamate and piperacetazine antagonized the anorectic effect of d-amphetamine. However, their antagonism of the motor stimulant effect of d-amphetamine was not uniform. Pentobarbital significantly increased but diazepam and piperacetazine significantly decreased the motor stimulant effect of d-amphetamine. Chlordiazepoxide and meprobamate did not alter the amphetamine effect on motor activity. 6 references. (Author abstract)

190260 Kelley, Diana L.; Mountford, Damon. 115 Meadowlane, Lansing, KS 66043 **The motivational consequences of cholinergic stimulation of the medial septal area.** Physiological Psychology. 2(2):101-103, 1974.

The motivational consequences of cholinergic stimulation of the medial septal area were examined in rats. Direct application of carbachol to the medial septal area of satiated rats produced large significant increases in drinking. Histamine produced a small and inconsistent increase in drinking, and

isoproterenol produced an inconsistent decrease in eating. Carbachol stimulated Ss performed significantly better on a brightness discrimination task than satiated controls, as measured by running and starting speeds, but did not differ from controls in number of correct choices. 9 references. (Author abstract)

190264 Pert, Agu; Avis, H. H. Biomedical Laboratory, Edgewood Arsenal, Edgewood, MD 21010 **Dissociation between scopolamine and mecamylamine during fear conditioning in rats.** Physiological Psychology. 2(2):111-116, 1974.

State dependent (dissociated) learning for both scopolamine (muscarinic anticholinergic) and mecamylamine (nicotinic anticholinergic) were examined in rats in a conditioned suppression task. In Experiment I, food deprived rats were trained to drink sweetened condensed milk in a test chamber for 8 days. On Day 9, all rats received a single electric shock in the same chamber 20 min after injections of scopolamine, mecamylamine, or saline. Three days later, subgroups were tested for conditioned suppression under the same drug condition, the other drug condition, or saline. Conditioned suppression was found in all groups except those trained under scopolamine or mecamylamine and tested under saline or the other drug condition. Experiment II controlled for some of the variables which may have produced dissociation in the first experiment. The findings are interpreted to imply the existence of two separate cholinergic (nicotinic and muscarinic) pathways which mediate fear conditioning. 23 references. (Author abstract modified)

190265 Barker, Lewis M.; Suarez, E. Martin; Gray, Don. Baylor University, Waco, TX 76703 **Backward conditioning of taste aversions in rats using cyclophosphamide as the US.** Physiological Psychology. 2(2):117-119, 1974.

Conditioned taste aversion was demonstrated in rats to result from a unconditioned stimulus (US) - conditioned stimulus (CS), or backward, conditioning procedure using a 75mg/kg cyclophosphamide injection as the US. The magnitude and resistance to extinction of the conditioned taste aversion was found to decrease monotonically when the US-CS intertrial interval was systematically varied from 1.0min to 4 h. It is argued that these results reflect truly associative, not pseudoconditioned, avoidance responses. 18 references. (Author abstract modified)

190266 Kahn, Jeffrey; Gorelick, David A.; Bridger, Wagner H. Swarthmore College, Swarthmore, PA 19081 **Mescaline facilitates retention of passive avoidance in rats.** Physiological Psychology. 2(2):120-122, 1974.

In a study of the effect of mescaline in the retention of passive avoidance, male hooded rats were given one trial of step through passive avoidance, then immediately injected with saline or mescaline (160micromoles/kg ip) and tested for retention 48 h later. Controls were given identical treatments, except that they did not receive footshock during the training trial. Groups receiving footshock showed significant learning and retention, with the mescaline group showing significantly better retention than the saline group. The no footshock groups showed no learning, with the mescaline group not differing from the saline. In a separate experiment, rats were given one trial of step through passive avoidance, then injected with saline or mescaline (160micromoles/kg ip) 72 h later and tested for retention 48 h after rejection. The mescaline group did not differ from the saline, indicating that mescaline did not have a 48 h proactive effect on performance in this task. 8 references. (Author abstract)

190275 Graf, Curtis L. State University of New York, Stony Brook, NY 11790 **Effects of scopolamine on inhibitory mechanisms.** Physiological Psychology. 2(2):164-170, 1974.

In a study of the effects of scopolamine on inhibitory mechanisms, scopolamine injected rats remained withdrawn from a novel chamber longer than controls under free exploratory conditions (Ss could withdraw into the home cage). This finding was interpreted to mean that scopolamine prevented the habituation of fear induced by the novel chamber. Under forced exploratory conditions (Ss had no opportunity to withdraw), scopolamine injected rats showed continuous general motor behavior rather than a within session decrease as found in control rats and as much within session decrease in locomotion, scanning, and object contact as did controls. These results were interpreted to mean that scopolamine produced a disinhibitory effect on general motor activity without interfering with behavioral response habituation. It was further suggested that the drug's disinhibitory effect on fear and general motor activity is due to the impairment of an inhibitory cholinergic system within the brain, but that this same cholinergic system does not mediate the inhibitory process underlying behavioral response habituation. 25 references. (Author abstract)

190309 Lassen, J. Buus. Department of Pharmacology, A/S Ferrosan, Sydmarken 1-5, DK-2860 Soeberg, Demark **Evidence for a noradrenergic and dopaminergic mechanism in the hyperactivity produced by 4, alpha-dimethyl-m-tyramine (H 77/77) in rats.** Psychopharmacologia (Berlin). 37(4):331-340, 1974.

The effect of 4,alpha-dimethyl-m-tyramine (H-77/77) on motility was investigated after injection to rats in a familiar cage. The doses produced hypermotility consisting of locomotion, sniffing, rearing, head twitch and various grooming movements. H-77/77 was administered to rats treated with various drugs affecting brain monamines. The H-77/77 hyperactivity was antagonized by: the tyrosine hydroxylase inhibitor H-44/68, the doapmine beta-hydroxylase inhibitor FLA 63, the (NA) noradrenalin receptorblockers aceperone and phenoxybenzamine, the thymoleptics imipramine, desipramine, chlorimiparmine, amitriptyline, nortriptyline, protriptyline, and doxepine, as well as the neuroleptics chlorpromazine thioridazine, perphenazine chlorprotixene, haloperidol, spiramide, pimozide and clozapine. The serotonin synthesis inhibitor H-69/17, the A-blocker propranolol and the antiparkinsonian agent benztropine showed no H-77/77 antagonism. These results indicate that release of catecholamines, especially NA, is involved in the mediation of H-77/77 induced hypermotility and that NA membrane blocking thymoleptics inhibit uptake of H-77/77 into brain NA neurons. Activation of both NA and dopamine receptors are necessary for the production of the H-77/77 behavioral syndrome as selective blockade of either system can prevent it. 37 references. (Author abstract modified)

190315 Ferraro, Douglas Peter; Grilly, David M. Department of Psychology, University of New Mexico, Albuquerque, NM 87131 **Effects of chronic exposure to delta9-tetrahydrocannabinol on delayed matching-to-sample in chimpanzees.** Psychopharmacologia (Berlin). 37(2):127-138, 1974.

The effects of chronic exposure to delta9-tetrahydrocannabinol (THC) on delayed matching to sample were examined in chimpanzees. Three groups of four chimpanzees were trained on a 20 sec delayed matching-to-sample task and then were exposed to a 152 day chronic drug regimen. The initial administrations of the drug before but not after each session

produced a significant decrease in matching to sample accuracy. During the course of the chronic drug regimen, animals in the experimental group who received a dose of THC prior to each daily session, recovered very slowly from this initial impairment in matching to sample performance. The extent to which the experimental animals recovered seemed to depend upon their prexeperimental drug histories. The drug experienced animals developed complete tolerance within five weeks while the previously drug naive animals did not so do even after five months exposure to the drug. No residual or long-term effects were observed following termination of the chronic drug regimen. 22 references. (Author abstract modified)

190317 Colasanti, Brenda K.; Craig, Charles R.; Hartman, Elizabeth R. Department of Pharmacology, West Virginia University Medical Center, Morgantown, WV 26506 **Differential effects of pentylenetetrazol on REM sleep in niave and cobalt-epileptic rats.** Psychopharmacologia (Berlin). 37(2):151-157, 1974.

The differential effects of pentylenetetrazol on rapid eye movement (REM) sleep were examined in niave and cobalt epileptic rats. Chronic experimental epilepsy was produced in adult female Sprague-Dawley rats by the implantation of cobalt wire into the right parietal cortex. Rats treated similarly with glass rods were used as controls. Administration of pentylenetetrazol at a dose of 15mg/kg every 15 min until the appearance of convulsions resulted in the lowering of the chemical seizure threshold expected for the cobalt treated rats, with only two injections of the drug required in contrast to the three to four injections needed for the control rats. Analysis of the EEG recordings collected over the 24 h period after the first injection revealed the presence of a more pronounced suppression of rapid eye movement (REM) sleep in the cobalt epileptic rats. This effect was found to e due to a reduction in the total b number of REM sleep episodes, while the duration of the individual episodes remained unchanged. The latencies to REM onset in these rats, moreover, wer markedly reduced. 24 references. (Author abstract modified)

190319 Dantzer, R.; Baldwin, B. A. Station de Pharmacologie 180, chemin de Tournefeuille, F-31300 Toulouse, France **Effects of chlordiazepoxide on heart rate and behavioural suppression in pigs subjected to operant conditioning procedures.** Psychopharmacologia (Berlin). 37(2):169-177, 1974.

The influence of chlordiazepoxide on response suppression and heartrate (HR) changes were examined in pigs submitted either to conflict conditioning or to a nonreinforcing procedure. Conflict behavior was evidenced by the suppression of operant responding and the occurrence of a marked decrease in heartrate during the presentation of the conditioned stimulus. Pigs in the nonreinforcement procedure showed no consistent changes in heartrate although an important decrease occurred in response rate. Chlordiazepoxide was administered in order to establish whether it would attenuate the response suppression in either procedure. The drug produced a weak attenuation of conflict in terms of the operant and heartrate responses at the maximum dose used (20mg/kg) and a small disinhibiting effect on the nonreinforced responding at 10mg/kg. 16 references. (Author abstract)

190330 Marcus, Richard; Kornetsky, Conan. Behavioral Pharmacology Laboratory, Boston University School of Medicine, 80 E. Concord St., Boston, MA 02118 **Negative and positive intracranial reinforcement tresholds: effects of morphine.** Psychopharmacologia (Berlin). 38(1):1-13, 1974.

Negative (aversive) and positive (self-stimulation) intracranial reinforcement thresholds were determined in rats using a double staircase psychophysical procedure. Morphine raised aversive thresholds at all doses tested, while the drug lowered positive reinforcement thresholds at low or moderate doses. The results suggest the possible involvement of central motivational systems in the mediation of morphine induced analgesia, the narcotic high, and narcotic addiction. 33 references. (Author abstract)

190331 Morrison, Cathleen F. Tobacco Research Council, Glen House, Stag Place, London S.W.1, England **Effects of nicotine and its withdrawal on the performance of rats on signalled and unsignalled avoidance schedules.** Psychopharmacologia (Berlin). 38(1):25-35, 1974.

The effects of nicotine and its withdrawal on the performance of rats on one unsignalled and two signalled avoidance schedules were examined. Rats were trained while under the influence of nicotine on a Sidman avoidance schedule. When saline was subsituted for nicotine the animals which had been trained on an unsignalled schedule showed poor avoidance and took significantly more shocks than their saline trained partners. When the schedule included either a warning signal preceding each shock or a feedback signal following each response this dependence did not develop. It is suggested that dependence on nicotine is related to the stressfulness of the situation and that the behavioural disruption found in its absence is due to an accentuation of the normal warmup process and not to dissociation of learning. 17 references. (Author abstract)

190332 Morrison, Cathleen F. Tobacco Research Council, Glen House, Stag Place, London, S.W. 1, England **Effects of nicotine on the observed behaviour of rats during signalled and unsignalled avoidance experiments.** Psychopharmacologia (Berlin). 38(1):37-46, 1974.

Rats which had been chronically injected with nicotine or with saline during avoidance training were observed during subsequent avoidance experiments. Among those trained and tested on an unsignalled schedule lever-holding and crouching were frequent and the stimulant effects of nicotine, though consistent, were small. When a warning signal preceded each shock or a feedback signal followed each response lever holding and crouching were reduced. The rats tested with saline were inactive but they tended to lie down rather than crouch during their periods of immobility. Nicotine treated rats in the signalled experiments were active with high levels of sniffing and grooming behavior. It is suggested that the lever holding and crouching in the unsignalled experiment were both aspects of freezing behavior. 9 references. (Author abstract)

190333 Driscoll, P.; Battig, K. Vet.-Physiol. Institute der University Zurich, Winterthurstrasse 260, CH-8057 Zurich, Switzerland **Effects of nicotine on the shuttlebox behavior of trained guinea pigs.** Psychopharmacologia (Berlin). 38(1):47-54, 1974.

The comparative effects of three doses of nicotine (0.075, 0.15 and 0.3mg/kg) were measured on the shuttlebox behavior of highly trained guinea pigs, using 50 trial sessions and a 15 sec conditioned stimulus - unconditioned stimulus interval. It was found that nicotine counteracted the characteristic intrasession performance decrement seen with this species and, in addition, that the various doses of nicotine could be differentiated from each other and the control (physiological saline) in this test. These results were obtained through the measurement of response latencies and the recording of inter-

trial responses which, for the purposes and conditions of this and future studies of this type, were shown to be more effective parameters than the measurement of avoidance frequency alone. 17 references. (Author abstract)

190334 Stewart, W. J.; Blampied, N. M.; Hughes, R. N. University of Tasmania, Tasmania **The effects of scopolamine on performance on a geometric progressive ratio schedule.** Psychopharmacologia (Berlin). 38(1):55-66, 1974.

The effects of the anticholinergic drug, scopolamine, on performance on a geometric progressive ratio schedule were examined in rats. Rats were trained to respond on a geometric progressive ratio schedule until performance was stable. They were then injected with the anticholinergic drug scopolamine at doses of 0.05, 0.1, 0.25, 1.0and 2.0mg/kg. Control animals were administered atropine methyl nitrate (1-2mg/kg). Increasing doses of scopolamine typically produced first an increase, then a decrease in behavior compared with baseline levels, measured by total number of responses, total number of reinforcements, and final completed ratio, per session. Atropine methyl nitrate had no effect on the behaviour of the control animals. This indicates that the effects of scopolamine are due to its central action. The inverted-U dose response curve found for scopolamine resembles that found for chlordiazepoxide, phenobarbital, and d-amphetamine on progressive schedules. 35 references. (Author abstract)

190335 Goudie, A. J.; Taylor, M.; Wheeler, T. J. University College of North Wales, Bangor, Caernarvonshire, Wales **Chronic anorexic and behavioural effects of the fenfluramine metabolite, norfenfluramine: an evaluation of its role in the actions of fenfluramine.** Psychopharmacologia (Berlin). 38(1):67-74, 1974.

The anorexic and behavioral effects of Norfenfluramine were studied in rats. Two separate experiments were conducted involving administration by intraperitoneal and subcutaneous routes respectively. Behavioral effects were assessed by time sampling categorisation on days 1 and 14 of a 20 day chronic study and anorexic effects by daily weighing. Norfenfluramine was found to be a potent anorexiant, to which tolerance is established fairly quickly. It was also found to possess sedative properties after acute administration, but marked stimulant properties after 14 days chronic administration. The results implicate Norfenfluramine in the anorexic and behavioral effects of Fenfluramine, and provide indirect confirmation of the suggestion that Fenfluramine may have chronic stimulant properties. 29 references. (Author abstract modified)

190696 Murphree, Oddist D.; DeLuca, Donald C.; Angel, Charles. Veterans Administration Hospital, North Little Rock, AR **Psychopharmacologic facilitation of operant conditioning of genetically nervous catahoula and pointer dogs.** Pavlovian Journal of Biological Science. 9(1):17-24, 1974.

The genetic factor underlying the disturbed behavior of E-line pointer bird dogs and catahoulas, and the psychopharmacologic conditioning used to restore integrated adaptive functioning were studied. The results of these experiments show that: 1) even dogs with the most severe schizokinetic disabilities of many years' duration have learned the operant conditioning; 2) however, it was and has remained necessary to facilitate both behavior shaping and nearly all later performances throughout the following year with benzodiazepine tranquilizers and these were far superior to any of these several other drugs tested; and 3) neither gradual or rapid withdrawal, nor sudden stopping of benzodiazepines allowed the dogs to continue the conditioned activity. In fact, during withdrawal of the drug, performance seemed to parallel blood levels. 14 references. (Author abstract modified)

190698 Livingston, Andrew, Jr. Pavlovian Research Laboratory, VA Hospital, Perry Point, MD **Inability to condition a peripheral activating drug.** Pavlovian Journal of Biological Science. 9(1):35-45, 1974.

The ability and mechanism of the kidneys to form CRs is surveyed. The production of glycosuria produced by peripheral stimulation cannot be conditioned. These experiments on animals show that glycosuria produced by tubular inhibition (phloridzin) cannot become a conditional response. One explanation of this failure to form a CR is that phloridzin acts peripherally rather than centrally. 10 references. (Author abstract modified)

191120 Poshivalov, V. P. First Leningrad I. P. Pavlov Medical Institute, Leningrad **/Psychotropic effect of analgesics and neuroleptics on a model of investigatory behavior changed by pain./** Izucheniye psikhotropnogo effekta anal'getikov i neyroleptikov na modeli issledovatel'skogo povedeniya, izmenennogo bol'yu. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(8):72-75, 1973.

The effect of analgesics (phentanyl, morphine) and neuroleptics (droperidol, chlorpromazine) on the exploratory behavior of white rats in a new situation and subject to pain stimulus, and on the dynamics of affective manifestations of the pain response, were studied. Small doses of phentanyl and droperidol had an insignificant effect on the initial reaction to pain but increased investigatory activity before the stimulus, decreased it after. Larger doses of neuroleptics reduced but did not block the pain reaction; they also reduced coordination and investigatory activity. Further increases in dosage failed to completely suppress affective behavior and activity. Large doses of analgesics completely blocked the pain reaction; morphine activated exploration, but it was aimless. The drugs affected the most highly integrated components of behavior, including motivation, as well as pain response. 5 references.

191141 Mehar, G. S.; Parker, J. M.; Tubas, T. Dept. of Pharmacology of Western Ontario, London, Ontario, Canada **Interaction between alcohol, minor tranquilizers and morphine.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):70-74, 1974.

Interrelationships between diazepam, a minor tranquilizer of the benzodiazepine type, ethanol and morphine were investigated in rats responding to electric foot shock. The effect on the threshold at which the rats responded is discussed for each drug individually and in combination. 5 references.

191211 File, Sandra E. Department of Psychology, City of London Polytechnic, Whitechapel High St., London E1 7PF, England **Changes in orienting and habituation in the rat following administration of chlorpromazine.** Quarterly Journal of Experimental Psychology (Cambridge). 26(1):125-130, 1974.

The possibility that orienting and habituation can be affected independently in a situation which gave a higher level of responding under the effects of chlorpromazine and a more precise control over the stimulus input was investigated in rats. Chlorpromazine (0.5- 3.0mg/kg) significantly reduced orienting to a novel auditory stimulus, but subsequent habituation after repeated presentations of the stimulus was not presented nor significantly impaired. Results support the suggestion that the mechanisms underlying orienting and habituation are independent. 12 references. (Author abstract modified)

191367 Sharpe, Lawrence G.; Garnett, Janie E.; Cicero, Theodore J. Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Analgesia and hyperreactivity produced by intracranial microinjections of morphine into the periaqueductal gray matter of the rat.** Behavioral Biology. 11(3):303-313, 1974.

The effects of intracranial microinjections of morphine into the periaqueductal gray matter were examined in the rat. Three to six micrograms of morphine injected in a 0.5microliter volume produced a marked increase in hot plate reaction time when injected into a circumscribed region of the periaqueductal gray matter ventral to the cerebral aqueduct encompassing the dorsal raphe nucleus and bordering tissue. Microinjections of low doses of morphine in other midbrain loci produced less effective antinociceptive activity or no analgesia at all. Higher doses of morphine eliminated the pain response to limb pinching, but in addition caused rats to become hyperreactive. Death resulted in seven of these hyperreactive rats. Although mild hyperactivity, i.e.,spontaneous motor activation, was frequently observed when 3 micrograms of morphine was microinjected into more lateral midbrain sites, this dose elicited little or no hyperreactivity. These results suggest morphine and electrical stimulation have similar mechanisms of action in producing analgesia when these active midbrain sites are involved. 34 references. (Author abstract modified)

191375 Gluck, John P.; Ferraro, Douglas Peter. Department of Psychology, University of New Mexico, Albuquerque, NM 87131 **Effects of delta9-THC on food and water intake of deprivation experienced rats.** Behavioral Biology. 11(3):395-401, 1974.

The effects of delta9-tetrahydrocannabinol (THC) on food and water intake of deprivation experienced rats were examined. Two groups of 16 rats were placed on either a 23 hr food or water deprivation regimen for 150 days. For 12 days following this period of adaptation, half of the rats in each group were pretreated with an oral dose of 1.0milligram THC per kilogram of bodyweight which was administered immediately after the daily 1 hr access to food and water. During the 12 day treatment phase, all the rats were administered the drug dose 2 hours prior to the daily access period. The rats were returned to nondrug recovery conditions for 8 days. The amount of food and water consumed during the 1 hr access period was increased by THC throughout the treatment phase, regardless of the rats' deprivation or pretreatment drug conditions. 16 references. (Author abstract)

191378 Stein, Donald G. Clark University, Worcester, MA 01610 **The effects of early saline injections and pentylenetetrazol on Hebb-Williams maze performance in the adult rat.** Behavioral Biology. 11(3):415-422, 1974.

Albino rats were given intraperitoneal injections of either saline or 15mg/kg pentylenetetrazol (PTZ) from 15 to 35 days of age, and then again at maturity, prior to testing in a Hebb-Williams maze. Those animals given saline while immature and again as adults made more errors than rats never injected, or those receiving saline only as adults. Rats receiving PTZ during development and/or at maturity performed as well as nontreated controls, suggesting that the drug may have counteracted the disrupting effects of the early injections. Injections at maturity were given on alternate days of testing, and all rats, including noninjected animals, made significantly more errors on days in which treatments were given. It is concluded that even saline injections can have an immediate effect on performance, and can influence behavior of noninjected animals tested in the same apparatus. 25 references. (Author abstract)

191504 Wallach, Marshall B. Department of Pharmacology, Syntex Research Corporation, Palo Alto, CA **Drug-induced stereotyped behavior: similarities and differences.** Psychopharmacology Bulletin. 10(3):12-13, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, similarities and differences in stimulant drug induced stereotyped behavior were discussed, based on data obtained from rats, cats, dogs, and mice. Generally, the evidence supports a dopaminergic mechanism of action, although some of the findings are contradictory. Interactions of amphetamine induced stereotypy with cholinergic, anticholinergic, and antihistaminic agents, as well as the benzodiazepines, were also discussed. The total impression suggests that stereotypy is primarily a dopaminergic phenomenon, which is a good model of both human CNS stimulant induced paranoid psychoses and the schizophrenia - paranoid type.

191505 Ellinwood, Everett H., Jr. Behavioral Neuropharmacology Section, Department of Psychiatry, Duke University Medical Center, Durham, NC **Behavioral and EEG changes in the amphetamine model of psychosis.** Psychopharmacology Bulletin. 10(3):13-14, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, results of several investigations of behavioral and EEG changes using a chronic amphetamine intoxication paradigm in cats were described. The level of abnormal arousal produced by amphetamine was directly related to the degree of distorted behavior manifested. Although the data are preliminary, there are indications that there may be changes in the organizational gradients of electrical activity of the forebrain that are related to pacemaking activity. The major behavioral, as well as electrophysiological, changes noted in the chronic amphetamine intoxication appeared in the most intense stages of hyperarousal, and a likely mechanism of action was suggested. 6 references.

191520 Zigmond, Michael J.; Stricker, Edward M. University of Pittsburgh, Pittsburgh, PA **The effects on ingestive behaviors of damage to central dopamine-containing neurons.** Psychopharmacology Bulletin. 10(3):40-41, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, an investigation of the hypothesis that nigrostriatal dopamine (DA) bundle might mediate important behavioral contributions to homeostasis was reported. Support for the hypothesis was found in the observation of a profound aphagia and adipsia in rats when depletion of striatal DA by 6-hydroxydopamine (6-DA) is more complete (greater than 90%). Despite permanent loss of brain DA, there is recovery from the initial gross incapacitation towards more normal behaviors resembling that of rats with severe depletions. Several lines of evidence suggest that recovery of function is partly due to compensatory processes within the damaged DA system. Additional experiments indicate that there is a decreased affinity of amine for uptake into the nerve terminals contributing, in part, to the observed supersensitivity to L-DOPA. Overall results suggest that the behavioral component of homeostatic regulation is compromised following subtotal damage to the nigrostriatal DA bundle, that some recovery is possible due to gradual compensatory changes that can occur within un-

damaged fibers; and that residual deficits in ingestive behaviors reflect the inability of this repaired system to support increased DA release during pronounced stimulation.

191521 Moore, Kenneth E. Department of Pharmacology, Michigan State University, East Lansing, MI **Behavioral effects of direct and indirect acting dopaminergic agonists.** Psychopharmacology Bulletin. 10(3):41-42, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a study of the interactions of direct and indirect acting dopaminergic agonists (apomorphine and d-amphetamine) with the ascending dopaminergic nigrostriatal pathway was described. Dextroamphetamine caused locomotor stimulation through a dopaminergic mechanism and it facilitated the release of dopamine from terminals of nigrostriatal neurons. Apomorphine, however, stimulated postsynaptic dopamine receptors directly. Direct acting and indirect acting dopaminergic agonists could be easily distinguished by determining their effects on the circling behavior of mice with unilateral 6-hydroxydopamine induced lesions in the striatum. 3 references.

191527 Poschel, B. P. H. Parke Davis and Company, Ann Arbor, MI **Role of norepinephrine, dopamine, and serotonin in intracranial reward.** Psychopharmacology Bulletin. 10(3):46-47, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, experiments investigating the role of norepinephrine, dopamine, and serotonin in intracranial reward were summarized, in which attempts were made to determine: whether norepinephrine is excitatory to self-stimulation; whether serotonin in inhibitory to self-stimulation; whether the influence of norepinephrine and serotonin on stimulation is reciprocal; whether dopamine is essential to normal motor functions and enters into self-stimulation behavior but not into the underlying reward process per se; and whether the monoamine neurons of the forebrain serve as modulators of motivational and reinforcement thresholds. Overall results indicate the possibility of obtaining good self-stimulation from points in the brain which are not monoaminergic in the sense that the self-stimulation obtained from these points does not respond to monoamine manipulating drugs (L-DOPA, monoamine oxidase inhibitors, p-chlorphenylalanine, and 5,6-dihydroxytryptamine). The monoamine neurons of the forebrain cannot therefore be absolutely critical to self-stimulation, as they would be if they were actual reward neurons. The alternative notion that monoamine neurons simply modulate self-stimulation and other motivational thresholds is favored. 2 references.

191528 Pradhan, S. N. Howard University, College of Medicine, Washington, DC **Balance between acetylcholine, serotonin, norepinephrine, and dopamine in self-stimulation.** Psychopharmacology Bulletin. 10(3):47-48, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the involvement of central putative neurotransmitters, including acetylcholine, serotonin, norepinephrine, and dopamine, in self-stimulation was reported. Neuropharmacological and neurochemical studies indicate that self-stimulation behavior is facilitated by adrenergic and possibly dopaminergic mechanisms and depressed by cholinergic and serotonergic mechanisms. Interactions between two or more of these transmitters on neuroanatomical, neurophysiological, neurochemical, and neuropharmacological bases have also been noted. It is therefore difficult to conceive of insulated central functional compartments, each dealing with the effect on an individual transmitter in regulation of this behavior or other central functions. The behavior is apparently modulated by a balanced multitransmitter system rather than by individual transmitter components. The disturbance in the balance induced by hypoactivity or hyperactivity of an individual component or components of this system may lead to changes in self-stimulation behavior.

191629 Bert, J.; Balzamo, E. Institut de Neurophysiologie et de Psychophysiologie, CNRS, 31 Chemin Joseph-Aiguier, F 13274 Marseille, Cedex 2, France **/Differential effects of parachlorophenylalanine on sleep in two primates, Papio papio and Papio hamadryas/.** Differenciation des effets de la PCPA sur le sommeil de deux primates appartenant au genre papio. Electroencephalography and Clinical Neurophysiology (Amsterdam). 37(2):161-166, 1974.

The differential effects of parachlorophenylalanine (PCPA) on sleep in two primates was examined. PCPA induces a decrease in sleep duration in the baboon, but was found to be partly different in two species of baboons, Papio papio and Papio hamadryas. The differences seemed to be related to normal sleep characteristics proper to each species, suggesting a biochemical specificity in the functioning of anatomically identical nervous structures. The effects of 5-hydroxytryptamine were identical in the two species, but PCPA does not have the same effect upon the various stages of slow wave sleep. Stage two was particularly modified; the mean duration of its episodes increasing while their number remained unchanged. This suggests an inhibitory influence of the serotoninergic system upon the catecholaminergic arousal system. 14 references. (Author abstract modified)

191788 Mekhilane, L. S.; Allikmets, L. Kh. Laboratory of Psychopharmacology, Tartu University, Tartu, USSR **/Influence of psychotropic drugs on aggressiveness evoked by destruction of isolated structures of the forebrain./** Deystviye psikhotropnykh veshchestv na agressivnost' vyzvannuyu razrusheniyem otdel'nykh struktur perednego mozga. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (P. 129-140). Vol. 9.

The effect of psychotropic drugs on aggressiveness elicited by destruction of sections of the forebrain in rats was investigated. Vocalization, affective pose and attack behavior were observed in operated, hyperemotional and false operated rats. Both brain lesions and prolonged isolation elicited hyperoggressiveness. Levomepromazine was the most effective tranquilizer. Trimeprimine was effective only on those rats which had undergone lesions of the anterior cingular and olfactory bulb; it stimulated aggressive behavior among those subject to septal lesions and isolation. The role of various brain segments in integrating emotional behavior and the effect of psychotropic drugs on limbic structures are discussed. 37 references. (Author abstract modified)

191899 Davis, W. Marvin; Smith, Stanley G. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Positive reinforcing effects of apomorphine, d-amphetamine and morphine: interaction with haloperidol.** Pharmacologist. 16(2):193, 1974.

At the fall metting of the American Society for Pharmacology and Experimental Therapeutics, positive reinforcement afer small i.v. doses of apomorphine HCI (APO), d-amphetamine sulfate (AS), or morphine sulfate (MS) was demonstrated both

by self-administration (SA) behavior and by the establishment of a buzzer stimulus as a conditioned reinforcer through pairings of buzzer and drug infusions. Male albino rats were allowed to self-inject (SI) drug soutions during a 6 h session on a continuous reinforcement schedule. Both fatal and nonfatal levels of APO intake were accompanied by pronounced stereotypic behaviors, but these were not responsible for SI. Some individuals seemed to learn to regulate their SA so that toxic properties of APO were largely avoided. The possible dopaminergic basis of SA for all three drugs was tested by means of i.p. haloperidol (HAL) pretreatment. Drug associated reinforcement was prevented by HAL in the case of APO and AS, but not for MS. (Author abstract modified)

191902 Friedler, G. Boston University School of Medicine, Boston, MA 02118 **Effect of pregestational morphine administration to mice on behavior of their offspring.** Pharmacologist. 16(2):203, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of parental exposure to morphine (M), prior to mating, on later response to M of their offspring was reported. Mature male and female mice Charles River strain, were injected s.c. with saline (C) or M twice daily for 5 days with the M increased in increments from 120mg/kg to a maximum of 240mg/kg. At 5 days following injections, 4 groups of mice were mated: Group 1, M males and C females; Group 2, M females and C males; Group 3, M males and M females; Group 4, C males and C females. Adult offspring from the four treatment groups were evaluated for their response to a 10mg/kg test dose of M using the shock attenuator precedure as a measure of drug effect. A significant decrease in maximum M effect was observed in both Groups 2 and 3 when compared with Group 4. A decrease in duration of M action was apparent in Group 1 although peak M effect did not differ from controls. The study suggests that pregestational M can alter the behavior of offspring and that effects may vary depending upon the sex of the treated parent. (Author abstract modified)

191914 Leith, Nancy J.; Barrett, Robert J. Vanderbilt University, Nashville, TN 37240 **Amphetamine's effects on self-stimulation: development of tolerance and post-drug depression.** Pharmacologist. 16(2): 215, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the development of tolerance and postdrug depression following amphetamine self-administration in the rat were reported. Rats implanted with bipolar electrodes in the median forebrain bundle were trained to self-stimulate and the current intensity was adjusted to levels which were minimally reinforcing. D-amphetamine (dA) produced marked increases in responding. With increasing current intensity, responding returned to high rates, indicating the animals were not physically debilitated. Further testing showed the minimal intensity which would support self-stimulation was markedly higher, indicating postamphetamine depression. Depression occurred prior to the development of tolerance. (Author abstract modified)

191915 Tessel, R. E.; Woods, J. H. University of Michigan Medical School, Ann Arbor, MI 48104 **Structural relationship between meta-subsituted N-ethyl amphetamines and self-administration in rhesus monkeys.** Pharmacologist. 16(2):215, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, doses of N-ethyl amphetamine (NEA) and its meta-fluoro (FEA), meta-bromo (BEA), meta-iodo (IEA) and meta-methyl (MEA) derivatives were substituted for response contingent intravenous injections of cocaine to determine the ability of these compounds to reinforce fixed-ratio 30 responding in rhesus monkeys. All compounds except IEA maintained stable responding at rates higher than saline when each dose was available for at least 14 sessions. With NEA and FEA the maximum rates occurred at 0.03mg/kg/injection; with BEA and MEA, maximum rates occurred at 0.10mg/kg/injection. IEA failed to reinforce responding even though in other monkeys it had a potency comparable to that of a self-administered drug, BEA, and a rapid onset of behavioral action in suppressing fixed-ratio 30 food reinforced responding. Findings indicate that substituent size influences the extent to which these compounds can function as reinforcers. (Author abstract modified)

191916 Gonzalez, Fernando A.; Goldberg, Steven R. Harvard Medical School, Boston, MA 02115 **Behavioral effects of cocaine compared under two schedules of food presentation in the squirrel monkey.** Pharmacologist. 16(2):215, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the behavioral effects of cocaine compared under two schedules of food presentation in the squirrel monkey were reported. Cocaine produced only dose related decreases in mean response rate under the FR schedule. Under the second order schedule, however, intermediate cocaine doses increased mean response rate about 80%, while the high dose decreased mean response rate. The time course of cocaine's effects was studied under the second order schedule during 180 min sessions. Intermediate cocaine doses increased responding early in the session; the high 3mg/kg dose decreased responding early in the session but markedly increased it late in the session. Cocaine may either increase or decrease responding depending on the dose, the time since injection and the schedule of reinforcement. (Author abstract modified)

191917 Vogel, Richard A.; Annau, Zoltan. Johns Hopkins University, Department of Environmental Medicine, Baltimore, MD 21205 **The comparative effects of pentobarbital and d-amphetamine on a short term memory task in baboons.** Pharmacologist. 16(2):216, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the comparative effects of pentobarbital and d-amphetamine in a short-term memory task in baboons were reported. Pentobarbital decreased accuracy in a memory task in a dose related manner and increased variability of response patterning. The low dose of amphetamine increased accuracy while the higher doses decreased accuracy as well as the number of self-initiated trials. All doses of d-amphetamine decreased variability of response patterning. (Author abstract modified)

191919 Yokel, Robert A. Center for Research on Drug Dependence, Sir George Williams University, Montreal, Canada **Pimozide, l-propranolol and phentolamine effects on amphetamine self-administration by the rat.** Pharmacologist. 16(2):216, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, pimozide, l-propranolol and phentolamine effects on amphetamine (A) self-administration by the rat were reported. l-Propranolol had little effect on the rate of A self-administration. The largest dose of phentolamine decreased response rate by 50% for about 4 hours. No change was seen in the stereotypic behavior normally accompanying A self-administration. Pimozide increased

response rate for A up to 300%, in a dose dependent fashion. After the initial increase in rate, rats stopped responding for A after 0.5mg/kg pimozide and stereotypic behavior was no longer seen. The effect of pimozide on A self-administration was similar to that seen when the injection dose of A is decreased (rate increase), or replaced by saline (rate increase followed by response termination). This suggests a role for dopamine in the regulation of intake and the reinforcement effects of amphetamine. (Author abstract modified)

191926 Goldberg, Steven R.; Morse, W. H.; Goldberg, D. M. Laboratory of Psychobiology, Harvard Medical School, Boston, MA 01772 **Naltrexone and naloxone: agonist and antagonist effects on key-press responding of pigeons maintained under a multiple schedule of food presentation.** Pharmacologist. 16(2):226, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of naltrexone and naloxone were compared in pigeons responding under a multiple fixed-interval (FI), fixed-ratio (FR) schedule of food presentation. Intramuscular doses of naloxone or naltrexone increased FI and FR responding of some pigeons; increases in responding were larger after naloxone than after naltrexone. Both naltrexone and naloxone decreased FI and FR responding and also produced tremors and vomitting. When studied in combination with a 10mg/kg dose of morphine that almost completely suppressed both FI and FR responding, naltrexone was approximately 10 fold more potent than naloxone in antagonizing the rate decreasing effects of morphine. Naltrexone doses as low as 0.01mg/kg completely antagonized the rate decreasing effects of 10mg/kg morphine; in contrast, partial antagonism of morphine's rate decreasing effects first occurred at a dose of 0.1mg/kg naloxone and complete antagonism occurred at a dose of 1mg/kg naloxone. (Author abstract modified)

191934 Gorelick, D. A. Albert Einstein College of Medicine, Bronx, NY 10461 **Interaction of mescaline and stress on shuttlebox escape/avoidance in rats.** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics. It was hypothesized that stress is an important factor in determining whether hallucinogens have excitatory or inhibitory effects on animal behavior. Male hooded rats were trained to high, stable baseline rates of avoidance, then given each of four treatments at 6 day intervals after returning to baseline avoidance rates: 1) saline; 2) saline + stress; 3) mescaline; 4) mescaline + stress. Treatments 1 and 2 had no effect on avoidance rate. Treatments 3 and 4 significantly decreased avoidance rate, with the latter causing significantly more decrease than the former. None of the treatments affected intertrial crossings of the shuttlebox. These results are inconsistent with the hypothesis that stress is the crucial factor in causing hallucinogens to have excitatory effects on animal behavior. (Author abstract modified)

191935 Lu, Lee Jane W.; Wilson, Ann; Moore, Robert H.; Domino, Edward F. Lafayette Clinic, Detroit, MI 48207 **Correlation between brain N,N-dimethyltryptamine (DMT) levels and bar pressing behavior in rats: effect of MAO inhibition.** Pharmacologist. 16(2):237, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a fluorometric assay to determine the actual tissue levels of dimethyltvyptamine (DMT) upon the administration of different dosages of DMT. The half-life of DMT is approximately 12.5min in brain and 7.4min in liver. Pretreatment with iproniazid 16 hr prior to DMT administration significantly increased the half-life of DMT, both in brain and in liver. It was possible to detect DMT in brain and liver 3 min after the administration of 1mg/kg. The brain concentration of DMT was below threshold for disruption of bar-pressing. (Author abstract modified)

191939 Altshuler, H. L.; Deneau, G. A.; Weaver, S. S.; Roach, M. K. Baylor College of Medicine, Houston, TX 77025 **Intragastric self-administration of psychoactive drugs in the rhesus monkey.** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a technique was evaluated which allows rhesus monkeys to self-administer (SA) psychoactive compounds directly into their stomachs (GSA). A gastric cannula was implanted into the greater curvature of the stomach and most other technical details were similar to intravenous self-administration (IVSA). Alcohol (ALC), pentobarbital (PB) and methadone (MD) were used to evaluate the usefulness of the model. The acquisition of GSA behavior was slower than IVSA but, once acquired, the GSA patterns remained consistent and predictable for each drug and monkey. MD GSA patterns were characterized by steadily increasing levels of drug intake. PB GSA was characterized by a relatively stable daily intake and occasional days of high drug intake. ALC GSA patterns were characterized by occasional days of voluntary abstinence and others of very high intake levels. These studies indicate that GSA is a useful animal model for studies of the abuse of alcohol and other drugs consumed orally by man. (Author abstract modified)

191940 Collins, R. James; Weeks, James R. Upjohn Company, Kalamazoo, MI 49002 **Alpha-methyl-p-tyrosine inhibition of self-administered intravenous morphine and oral water in rats.** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, alpha-methyl-p-tyrosine (AMPT) inhibition of self-administered intravenous morphine (MS) and oral water in rats was reported. AMPT methyl ester was infused for 2 days to MS addict rats without effect on MS intake. Naive rats were infused with AMPT or vehicle for 5 days, and after 2 days started MS self-administration. Controls were 2 groups (N=10) of naive rats self-administering saline. On the last day the AMPT and vehicle groups took 18.3and 18.7saline injections, respectively. The AMTP and vehicle experimental groups took 18.9MS injections, while the vehicle infused experimental group took 62.6MS injections, respectively. Two more groups of naive rats were infused with AMPT or vehicle. After 2 days infusion a response now delivered 0.2ml of water into a cup. On the last day, 14/15 vehicle rats had learned to obtain water whereas only 9/17 AMPT rats had so learned. Subsequent infusion of AMPT for 2 days had no effect on water intake. These experiments support the concept that the effect of AMPT on MS and water reinforcements in rats may primarily affect learning. (Author abstract modified)

191941 Grove, Robert N. University of Chicago, Chicago, IL 60637 **Differential sensitivity of methohexital self-administration to shock punishment early vs. late in session.** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the differential sensitivity of methohexital self-administration to shock punishment early vs late in the session was reported in rhesus monkeys. Two shock conditions were superimposed. In one condition the

SD1: shock condition, only responses in the first, third and fifth 30cminute components were shocked while in the other condition, SD2: shock, only responses in the second, fourth and sixth components were shocked. The SD1: shock procedure resulted in nearly total elimination of drug intake across the entire 3 hour session for all subjects. The same animals showed no effects when the same shock intensity was delivered for each response in the SD2 components. Thus while shock punishment may be effective in suppressing behavior which leads to methohexital intake (SD1 procedure), the sensitivity of behavior to punishment procedures may be attenuated by immediately prior self-administered drug (SD2 procedure). (Author abstract modified)

191944 Hirschhorn, Ira D.; Hayes, Ronald L.; Rosecrans, John A. Medical College of Virginia, Richmond, VA 23298 **Discriminative control of behavior by electrical stimulation of the dorsal raphe nucleus: generalization to lysergic acid diethylamide (LSD).** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, experiments to determine whether electrical stimulation of the dorsal raphe nucleus could serve as a discriminative stimulus and the interaction of certain drugs with this stimulus were reported. Following recovery from surgery, the rats were trained to press both bars of an operant chamber and discrimination training was begun. Depression of one of the levers resulted in food reinforcement in the presence of brain stimulation. Responses on the opposite lever were reinforced in the absence of brain stimulation. A high degree of discriminated responding rapidly occurred. Injections of morphine sulphate or LSD tartrate did not alter responding during stimulation. In the absence of stimulation, LSD, but not morphine, produced responses appropriate to electrical stimulation. These results indicate that electrical stimulation of the dorsal raphe nucleus and LSD have similar stimulus properties. (Author abstract modified)

191952 Matsuzaki, M.; Okamoto, M. N.Y. State DACC Testing and Research Lab., Brooklyn, NY 11217 **Long-term alteration of sleep-wakefulness cycle during chronic pentobarbital dosing and withdrawal in cat.** Pharmacologist. 16(2):247, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of chronic pentobarbital dosing on sleep-wakefulness cycle during the treatment and the drug abstinence were studied. During the chronic treatment, states of physiological sleep (slow wave sleep (SWS) and paradoxical sleep (REM)) were markedly suppressed. Following abrupt drug withdrawal, various withdrawal signs which include grand mal type seizures occurred within 20 to 24 hours and continued for 4-7 days. SWS and REM were completely absent while animals were displaying most severe withdrawal signs (2-4 days). SWS gradually appeared with the diminution of overt abstinence signs; 2-3 days later, REM emerged and continued to increase to rebound for 5-7 days. Complete recovery of the sleep-wakefulness cycle occurred in 3 weeks. (Author abstract modified)

191953 Boisse, N. R.; Okamoto, M. Cornell University Medical College, New York, NY 10021 **Comparison of barbital & pentobarbital physical dependence in the cat.** Pharmacologist. 16(2):247, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the abstinence characteristics of short and long-acting barbiturates were compared in cats. Kinetic analysis of blood levels shows the fractional change in blood concentration of barbital (B) and pentobarbital (P) to be the same reinforcing treatment equivalency. P abstinence is most severe culminating in a 100% incidence of convulsions and 30% death. In contrast, all cats survived B abstinence and seizures were usually absent. Results of substitution wherein B replaced P or P replaced B following chronic treatment suggest an important role for elimination kinetics (t l/2) in abstinence. To exclusively manipulate t l/2, a schedule of lst order dose reduction was developed to extend P t l/2 to that of B. These findings confirm the important role of t l/2 in the overt expression of an underlying dependence. (Author abstract modified)

191966 Heyman, I. A.; Bunnell, P. R.; Rosenkrantz, H.; Braude, M. C. Mason Research Institute, Worcester, MA **Comprehensive behavioral assessment of the effects of delta9-tetrahydrocannabinol in rats.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, physiological and behavioral parameters were evaluated for the development of tolerance to delta9-tetrahydrocannabinol (THC) by modifications of established observational techniques. Exploratory activity, respiration rate, ataxia, relaxation, corneal reflex and irritability were reliable indicators of tolerance. An increase in the number of animals exhibiting aberrant behavior was observed although a decrease in the duration of depressant effects occurred as the dose of THC was increased. Maximum changes occurred in the following indices: passivity at 10mg/kg, irritability at 20mg/kg, transfer arousal, hypersensitivity, corneal reflex and wire maneuver at 40mg/kg, and ptosis, relaxation, pinna reflex, visual placing and bizzare behavior at 80mg/kg. Results indicated that tolerance developed only to several specific depressant effects of THC in this observational behavioral screen of marihuana effects. (Author abstract modified)

191967 Borgen, Lowell A.; Shumway, John. Department of Pharmacology and Toxicology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **Comparative effects of delta9-tetrahydrocannabinol (delta9-THC), cannabidiol (CBD), and cannabinol (CBN) on timing behavior in rats.** Pharmacologist. 16(2):260, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the comparative effects of delta9-tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN) were reported. THC at doses of 2.5and 5mg/kg produced increased bar press response rates and decreased the number of reinforcements received. At 10mg/kg THC both response rate and number of reinforcements decreased while 1.25mg/kg showed no effect. CBN at 5 and 10mg/kg increased DRL response rate and decreased frequency of reinforcement. Higher doses of CBN depressed both response rate and reinforcement frequency. Pretreatment with CBD at 10 and 25mg/kg was without discernible effect whereas doses of 50 and 100mg/kg resulted in decrements in both response rate and number of reinforcements. (Author abstract modified)

191972 Downs, David A.; Woods, James H. University of Michigan Medical School, Ann Arbor, MI 48104 **Effects of morphine, pentazocine, and naloxone on operant responding in monkeys and pigeons.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of morphine, pentazocine, and naloxone on operant responding in monkeys and pigeons were reported. Morphine, pentazocine, and naloxone generally had dose dependent response rate decreasing ef-

fects in fixed-interval and fixed-ratio components. The decreasing order of potency in suppressing responding was morphine pentazocine naloxone except in fixed-ratio components in pigeons, where morphine and pentazocine were equipotent. Antagonism of the response rate decreasing effects of morphine by naloxone became more complete as naloxone dose increased. Antagonism of the response rate decreasing effects of pentazocine by naloxone was greatest at low naloxone doses in monkeys and in pigeons. In both monkeys and pigeons, antagonism by naloxone was less complete at high doses of pentazocine than at comparably high doses of morphine. (Author abstract modified)

191973 Wenger, Galen R. Department of Pharmacology, Harvard Medical School, Boston, MA 02115 **Effects of phencyclidine and ketamine on food maintained behavior in the pigeon.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of phencyclidine and ketamine on food maintained behavior in the pigeon were reported. Both phencyclidine (PCD) and ketamine (KT) increased rates during the fixed-interval (FI) component only and decreased fixed-ratio (FR) rates more than FI rates with increasing doses. The rate increases in the FI component after PCD, unlike KT, depended on the control rate of responding (rate dependency). Other pigeons were trained on a multiple FR-30 schedule of food presentation. In one component high rates of responding were maintained. In the other component each response produced a 30 msec, 6 mA electric shock that suppressed behavior (punishment). Both PCD and KT produced increased response rates in the punished component of the schedule with little effect on the unpunished component. These effects are pentobarbital like. PCD and KT have a distinctive spectrum of behavioral effects. (Author abstract modified)

191974 Ts'o, Timothy O. T. Saginaw Valley College, Saginaw, MI 48710 **Effects of chlorpromazine CPZ) and thioridazine performance and stimulus control behavior.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the sensitivity of performance and stimulus control to the action of chlorpromazine (CPZ) and thioridazine (TRZ) within the same experimental context was examined. A cued variable interval schedule with limited hold periods (LHP) was used. Male Long-Evans rats generated high rates of responding during the LHP and were significantly depressed by 1mg/kg CPZ and 4.4mg/kg TRZ. Their responses to the cues were significantly depressed by 4mg/kg of CPZ but not by 5.4mg/kg TRZ. It was concluded that the treatments with these drugs affected the rate of responding at lower doses and did not affect the stimulus control behavior until higher doses were given. (Author abstract modified)

191975 Markowitz, Robert A.; Marcus, Richard; Kornetsky, Conan. Boston University School of Medicine, Boston, MA 02118 **Effects of morphine sulfate on positively and negatively reinforced behavior in two strains of rats.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of morphine sulfate (MS) on positively and negatively reinforced behavior in two strains of rats were reported. In the CD strain animals, 5-10mg/kg MS impaired or abolished responding on both tasks, this effect beginning 15-20 min postinjection. The CDF rats, however, were resistant to doses of 5mg/kg MS. Doses ranging from 10-30mg/kg MS impaired responding; however, performance on the avoidance task appeared to be more susceptable to this drug induced disruption than was performance on the positive task. During certain time segments after injection, performance on the positive task remained near 100% correct while avoidance and escape responses on the negative task were completely abolished. (Author abstract modified)

191976 Weiss, L. R.; Krop, S. Drug Biology, FDA, Washington, DC 20204 **Comparative effects of some CNS-active drugs on learned and unlearned behavior in the hamster.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of some central nervous system active drugs on learned and unlearned behavior were compared. By age 35 days, singly caged hamsters of both sexes show a strong drive to move food pellets to a fixed place in their cages. This food hoarding activity (FHA) was quantified by measuring the time to move (MT) 20 pellets from the front to the rear (fixed place). Prenatal postnatal oral doses of d-amphetamine and fenfluramine to mothers, which severely reduce pup survival, had no effect on later FHA onset or learning T-maze avoidance - escape (TAE) in survivors. Both drugs inhibit FHA in adults at doses that have little effect on TAE. Scopolamine delays FHA at doses at which atropine does not, chlorpromazine blocks FHA at doses not affecting TAE, and reserpine causes long lasting FHA deficits. The results indicate that the hamster represents a new animal model, which is rapid, reliable and economical, for the study of drug action (useful and adverse) on learned and unlearned behavior. (Author abstract modified)

191977 Hine, B.; Wallach, M.; Gershon, S. NYU Medical Center, New York, NY 10016 **Drug-induced aggression in chicks: differential involvement of biogenic amines.** Pharmacologist. 16(2):263, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, studies were presented which evaluated drug induced aggressive pecking in pairs of neonate chicks as a model for identifying antidepressants and determined if different biogenic amines are involved in pecking induced by an antidepressant (imipramine-IMI) and a general CNS stimulant (d-amphetamine=AMP). Pecking was induced by a variety of test compounds including IMI, AMP, l-DOPA, and opipramol (a tricyclic anxiolytic), but not by pargyline, atropine, caffeine, or iprindole (a tricyclic indole antidepressant). Pretreatment of chick pairs with amine blocking agents before AMP or IMI revealed that haloperidol blocked AMP but not IMI pecking, while methysergide partially blocked and propranolol potentiated IMI pecking. The data implicate dopamine in AMP induced aggressive pecking and provide further evidence of a serotonin catecholamine influence in the action of IMI. (Author abstract modified)

191983 Carney, J.; Llewellyn, M.; Woods, J. M. University of Michigan, Ann Arbor, MI 48104 **Comparison of codeine and ethyl alcohol self-administration under a variable interval (VI) schedule in monkeys.** Pharmacologist. 16(2):264, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a comparison of codeine and ethyl alcohol self-administration under a variable interval (VI) schedule in monkeys was reported. Maximum response rates were maintained by 0.1mg/kg/inj of codeine and by 0.18gm/kg/inj of ethanol. Higher or lower doses resulted in lower rates of responding. The rate of both codeine and

ethanol reinforced responding progressively decreased throughout the 1 hour session. The frequency of codeine injections did not change throughout the session, while ethanol injections decreased in frequency similar to the decline in rate of responding. Replication of doses which maintained maximal rates resulted in a 2.5fold increase in ethanol reinforced response rates and no change in responding maintained by codeine. (Author abstract modified)

191991 McCoy, D. J.; Brown, D. J.; Forney, R. B. Indiana University School of Medicine, Indianapolis, IN 46202 **The effect of cannabinoid mixtures on the response to stimulant drugs in mice.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of cannabinoid mixtures on the responses to stimulant drugs in mice was reported. Male mice pretreated with cannabidiol (CBD), delta-9-tetrahydrocannabinol (THC), or a mixture or these two, were given one of three stimulant drugs: amphetamine, strychnine, or metrazol. Animals receiving amphetamine were observed for four hours in activity cages. Those receiving strychnine or metrazol were given doses in the lethal range and LD50's were calculated. CBD did not alter activity in mice receiving amphetamine. THC, at first, depressed activity and then prolonged the increase in activity. The mixture of the two cannabinoids gave a similar effect to the THC alone. The LD50 of strychnine was decreased by CBD but not significantly altered by THC. When both were given, the LD50 was not changed from control. Neither CBD nor THC alone in doses up to 50 mg/kg altered the LD50 of metrazol, but a combination of 50mg/kg of each given together increased the LD50. The data presented supports the hypothesis that CBD may alter the effects of THC, even at a central level. (Author abstract)

192009 Rech, R. H.; Gudelsky, G. Michigan State University, East Lansing, MI 48824 **Interactions between Ro4-1284 and d-amphetamine (dA) on shuttle-box avoidance in rats.** Pharmacologist. 16(2):307, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, d-amphetamine (dA) impaired acquisition (Acq) of shuttle box avoidance (SBA) by Ro4-1284 and the capacity of d-amphetamine or L-dopa to antagonize this impairment was reported. One hr training of saline injected rats resulted in SBA scores of about 50% over the last 20 trials. Subjects pretreated with Ro4-1284 showed essentially no SBA over the entire hr. Rats given Ro4-1284 and then dA showed normal levels (50%) of SBA Acq. This dose of dA when given alone to naive rats did not change Acq of SBA from that of controls. L-dopa, was not effective in antagonizing R04-1284 impairment of acquisition. The two higher doses of L-dopa suppressed SBA Acq when injected alone. The results indicate important differences in central stimulant properties between dA and L-dopa. (Author abstract modified)

192012 Thornburg, J. E.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **supersensitivity to dopaminergic agonists following withdrawal of a chronic diet containing haloperidol or pimozide.** Pharmacologist. 16(2):307, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, supersensitivity to dopaminergic agonists following withdrawal of a chronic diet containing haloperidol or pimozide is reported. Mice fed a diet containing 0.005% haloperidol or 0.01% pimozide for 5 or 10 days exhibited a significant increase in locomotor activity 2 days after withdrawal of the drug. The hyperactivity was not observed after a 1 or 3 day haloperidol containing diet and disappeared by 7 days after a 5 or 10 day diet. At 2 days after a 5 day diet of 0.005% haloperidol, the dose response curve for apomorphine stimulated motor activity shifted to the left. At 2 days after the haloperidol diet, apomorphine, ET-495 (piribedil) L-DOPA and d-amphetamine induced gnawing at doses lower than required in control mice. These results suggest that prolonged blockade of dopamine receptors in the brain causes the development of an increased sensitivity of the receptors. (Author abstract modified)

192014 Abdallah, Abdulmuniem, H.; White, Harold D. Dow Chemical Company, Midland, MI 48640 **Interaction of serotonin antagonists with 3',4'-dichloro-2-(2-imidazolin-2-YL-thio)-2-acetophenone hydrobromide (DITA) and D-amphetamine on certain behavioral parameters of male mice.** Pharmacologist. 16(2):307, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of serotonin antagonists on the behavioral activities of DITA and d-amphetamine was studied in male mice. The serotonin antagonists, methysergide, cyproheptadine and parachlorophenylalanine (p-CPA) failed to significantly modify the anorexigenic activity of either DITA or d-amphetamine. Methysergide caused d-amphetamine to significantly decrease spontaneous motor activity (SMA). The p-CPA caused DITA to significantly increase SMA. Cyproheptadine, alone or in combination with d-amphetamine or DITA significantly increased SMA. Methysergide caused the anorexigenic agents to significantly decrease the rearing behavior of mice, while p-CPA and DITA had no effect. d-Amphetamine caused hypothermia in mice treated with methysergide or with cyproheptadine. DITA caused hypothermia in saline treated mice and in those pretreated with cyproheptadine or with p-CPA. (Author abstract modified)

192016 Dubinsky, Barry; Karpowicz, J. K.; Sledge, Karey; Robichaud, Roger C. Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Differential increase of behavioral and extrapyramidal stimulating actions of neuroleptics by alpha-methyltyrosine pretreatment in rats.** Pharmacologist. 16(2):308, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the degree of enhancement of the behavioral (Sidman avoidance in nonlesioned Long-Evans rats) and the extrapyramidal stimulating (EPS) effects (in unilaterally caudate lesioned rats) of chlorpromazine (CPZ) and haloperidol (HP) by alpha-methyltyrosine methylester hydrochloride (AMT) pretreatment were reported. Compared with saline pretreated subjects, AMT augmented the behavioral effect of CPZ and of HP. Enhancement was relative to the dose of each neuroleptic. ED50 values for EPS after CPZ were similar but differed after HP in saline and AMT pretreated subjects. It may be possible to experimentally dissociate desirable from nondesirable actions of neuroleptics. (Author abstract modified)

192018 Gale, Karen; Horita, Akira. University of Washington, Seattle, WA 98195 **Dopamine agonist induced disorientation in a rat swimming task.** Pharmacologist. 16(2):308, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, dopamine agonist induced disorientation in a rat swimming task was described. Under the influence of d-amphetamine (AM) or apomorphine (APO) the swimming became random and apparently nondirected; swimming ability per se was not impaired however, and the

rats reached the ladder by chance after 10-60 sec. The AM and APO indiced disorientation was blocked by pretreatment with haloperidol or pimozide at doses which did not completely block APO induced stereotyped gnawing. A variety of compounds including scopolamine, phenoxybenzamine, clonidine, chlordiazepoxide, LSD, and 5-hydroxytryptophan, did not significantly affect the behavior of the rats in this task. Scopolamine pretreatment reduced the minimal effective dose of APO by 50-80%. The disorientation effect thus seems to be specific to stimulation of a dopaminergic system and subject to marked potentiation by cholinergic antagonism. (Author abstract modified)

192116 Gauron, Eugene F.; Rowley, Vinton N. Department of Psychiatry, University of Iowa, Iowa City, IA 52242 **Effects of chronic methylphenidate administration on learning and offspring behavior.** Journal of General Psychology. 91(first half):157-158, 1974.

Long-term effects of methylphenidate administration in infancy upon learning measured in adulthood, behavioral effects of dosage or duration of the drug, and cross-generational effects in undrugged offspring were explored, using litters of albino rats. Results indicate that methylphenidate when administered chronically within the dosage rate sampled did not affect learning as measured by avoidance conditioning. Dosage and duration did have an influence, with higher dosages and longer durations resulting in lessened body weights. Male offspring showed no evidence of cross-generational effects, but female drug offspring learned at a slower rate than the control group. 1 reference. (Author abstract modified)

192415 Horibe, M. Department of Pharmacology, Tokyo Medical College, Shinjuku, Tokyo, Japan **The effects of psilocybin on EEG and behaviour in monkeys.** Activitas Nervosa Superior (Praha). 16(1):40-42, 1974.

Spontaneous behavior was classified and recorded, and autonomic phenomena and responses to various sensory stimulations were observed in rhesus monkeys. After an intraperitoneal injection of psilocybin, only the dynamic behavior was observed. Psilocybin produced two phases of behavioral changes in monkeys, first a dynamic and then a static phase with intoxicated aphrodisiacal action. Neocortical EEG changes were correlated with behavior but not with the EEG of the hippocampus and amygdaloid complex in both monkeys and rabbits. In the interperiod between the two behavioral phases, a staggering gait was observed in monkeys which was specially correlated with EEG changes. 4 references.

192421 Niemegeers, C. J. E. Janssen Pharmaceutica, Beerse, Belgium **The predictive value of the anti-apomorphine test in dogs for neuroleptic therapy in man.** Activitas Nervosa Superior (Praha). 16(1):56-58, 1974.

The predictive value of the antiapomorphine test in dogs is reviewed in relation to neuroleptic therapy in man. The experimental method, the method of extrapolation and the reliability of the predictions were studied in rats. Haloperidol and pimozide were about equiactive orally and subcutaneously. Subcutaneously, haloperidol was much faster acting than pimozide. The recommended maintenance dosage schedule is two administrations a day of haloperidol and one of pimozide. 14 references.

192424 Muller-Calgan, H. Lab. of Comparative Neuro-Psychopharmacology, Dept. of Pharmacology, Medical Research Institute, E. Merck, Darmstadt, Germany **A pharmacological model with rhesus monkeys for the prediction of selective depression of psychic functions.** Activitas Nervosa Superior (Praha). 16(1):62-64, 1974.

Major and minor tranquilizers, antiemetics, muscle relaxants, hypnotics, anticholinergics, analgesics, and hypotensive drugs were tested on adult rhesus monkeys for spontaneous motor activity and induced threatening behavior. The depressant effect in therapeutic doses of drugs causing central depression was shown. A sedative effective was evident with small doses of thiethylperazine, scopolamine, morphine, and clonidine. Threat behavior was normally resistant to drug influence. In fact, only a few of the tranquilizers tested exhibited a complete inhibition of threat. 8 references.

192430 Kazdova, E.; Dlabac, A.; Benesova, O. Institute of Pharmacology, Medical Faculty of Hygiene, Prague, Czechoslovakia **The effect of octoclothepin and perphenazine on behaviour in rats with different exploration and defecation rates.** Activas Nervosa Superior (Praha). 16(1):73-75, 1974.

The effects of two neuroleptic agents on genetically selective rats were studied. After drugs the motility decreased in both groups, but in the animals with a high rate of exploration the central inhibitory action of both neuroleptics was significantly higher. No difference in motor activity was found between the rats selected for low and high rate of defecation in the control sessions, and neither the rearing nor the horizontal activity were influenced by neuroleptic treatment. No significant difference was found between the effects of octoclothepin and perphenazine. 3 references.

192565 Quimby, Kelvin L.; Aschkenase, Lea J.; Bowman, Robert E.; Katz, Jordan; Chang, Louis W. Psychology Department, University of Wisconsin, Madison, WI 53706 **Enduring learning deficits and cerebral synaptic malformation from exposure to 10 parts of halothane per million.** Science. 185(4151):625-627, 1974.

Chronic exposure of rats to 10 parts of halothane per million during early life produced later deficits in learning a shock motivated light - dark discrimination and a food motivated maze pattern, correlated with enduring synaptic membrane malformation in cerebral cortex. Adult exposure had no effect. Halothane may provide a useful analytical tool for brain study. The behavioral ultrastructural techniques also suggest a standard for assessing the safety of trace toxicants with central nervous system effects. 15 references. (Author abstract)

05 TOXICOLOGY AND SIDE EFFECTS

188430 Westheimer, Ruth; Klawans, Harold L. Chicago, IL **The role of serotonin in the pathophysiology of myocolonic seizures associated with acute imipramine toxicity.** Neurology. 24(4):387-388, 1974.

The effect of imipramine on 5-Hydroxytryptophan (5-HTP) induced myoclonus in guinea pigs was studied. Serotonin mechanisms in relation to infants' seizures and Down's syndrome were investigated in relation to the pathophysiology of imipramine induced myoclonus. It was discovered that neither imipramine nor subthreshold doses of HTP given alone had any obvious behavioral effect on young guinea pigs. Potentiation of 5-HTP induced myoclonus by imipramine was not blocked by phentolamine, propranolol, scopolamine, and chlorpromazine. These results suggest that serotonin plays a role in the myclonus associated with imipramine toxicity and that seizures may be treated with serotonin antagonists. This is also the first demonstration that imipramine does alter

serotonin related behavior in intact animals. (Journal abstract modified)

188689 Albin, Maurice S.; Bunegin, Leonid; Massopust, Leo C., Jr.; Jannetta, Peter J. Department of Anesthesiology, University of Pittsburgh School of Medicine, Pittsburgh, PA 15261 **Ketamine-induced postanesthetic delirium attenuated by tetrahydroaminoacridine.** Experimental Neurology. 44(1):126-129, 1974.

Ketamine hydrochloride (KH) induced postanesthetic delirium attenuated by tetrahydroaminoacridine (THA) is reported in dogs. Responses to THA were significant in factors concerning duration of anesthesia and emergence. THA given 2 min after KH showed a marked decrease in the duration of anesthesia compared to the KH alone. All treatment groups employing THA showed a significant narrowing in emergence time. Results indicate the reversal of the anesthetic effects of a parenteral agent. The THA-KH interaction significantly decreased abnormal autonomic, central and motor responses from KH control levels. 16 references.

188738 Wilson, Wilkie A.; Escueta, Antonio V. Epilepsy Center, VA Hospital, Durham, NC 27710 **Common synaptic effects of pentylenetetrazol and penicillin.** Brain Research (Amsterdam). 72(1):168-171, 1974.

The synaptic effects of pentylenetetrazol (PTZ) and penicillin were examined in the abdominal ganglion of Aplysia californica. During the control period, firing in L10 yielded short inhibitory postsynaptic currents (IPSC) in L3 and an excitatory postsynaptic current (EPSC) appeared after the right connective was shocked. When the cell was perfused with penicillin, the short IPSC was attenutated and the EPSC was not altered. Application of PTZ caused a selective reduction in the short IPSC and no change in its reversal potential. There were no changes in the long IPSC or EPSC. The results indicate a common synaptic effect of penicillin and PTZ; they selectively block a cholinergic short inhibitory postsynaptic potential. Is is suggested that these drugs are acting postsynaptically. 16 references.

188865 Maling, H. M.; Highman, B.; Williams, M. A.; Saul, W.; Butler, W. M., Jr.; Brodie, B. B. Laboratory of Chemical Pharmacology, National Heart and Lung Institute, NIH, Bethesda, MD 20014 **Reduction by pretreatment with dibenamine of hepatoxicity induced by carbon tetrachloride, thioacetaminde or dimethylnitrosamine.** Toxicology and Applied Pharmacology. 27(2):380-394, 1974.

The reduction by pretreatment with dibenamine of hepatotoxicity induced by carbon tetrachloride (CG14) thioacetamide or dimethylnitrosamine is reported. Pretreatment with debenamine protected rats against the hepatotoxicity of CCl4, thioacetamide, or dimethylnitrosamine, but not against allyl alcohol or bromobenzene. Protection was evident from reduced activity of plasma glutamic pyruvic transaminase and reduced liver necrosis as demonstrated by histologic evaluations. In rats pretreated with debenamine, LD50 values for CCl4 and thioacetamide were elevated and liver triglycerides after CCl4 and dimethylnitrosamine were reduced. Dibenamine protection against hepatotoxicity did not correlate with alpha-adrenergic receptor blockade. Similar pretreatment with 3 other alpha-adrenergic blocking agents, tolazoline, phenoxybenzamine, and EEDQ (N-ethoxycarbonyl-2- ethoxy-1,2-dihydroquinoline), failed to protect rats against CCl4 induced hepatotoxicity. 24 references. (Author abstract)

188872 Thompson, George R.; Fleischman, Robert W.; Rosenkrantz, Harris; Braude, Monique C. Abbot Laboratories, D-468, Abbott Park, North Chicago, IL 60064 **Oral and intravenous toxicity of delta9-tetrahydrocannbinol in rhesus monkeys.** Toxicology and Applied Pharmacology. 27(3):648-665, 1974.

Oral and intravenous toxicity of delta9-tetrahydrocannabinol in rhesus monkeys were studied. No deaths occurred in monkeys treated acutely po with up to 9000mg/kg, but all monkeys treated acutely iv with 128mg/kg, or more died from respiratory arrest and cardiac failure. In the subacute oral study two of eight monkeys treated with 500mg/kg/day became moribund on days 10 and 14, and one of six monkeys treated with 50mg/kg/day became moribund on day 16. In the subacute iv trials, two of four monkeys treated with 45mg/kg/day died on days 8 and 19 as a result of acute hemorrhagic pneumonia, but injection site edema, necrosis, ulceration and fibrosis also occurred. Behavioral and physiologic changes were similar in both studies. 32 references. (Author abstract modified)

188874 Desi, Illes; Gonczi, Lili; Simon, Gyorgy; Farkas, Ildiko; Kneffel, Zsuzsa. Department of Toxicology, National Institute of Public Health, Budapest, Hungary. **Neurotoxicologic studies of two carbamate pesticides in subacute animal experiments.** Toxicology and Applied Pharmacology. 27(3):465-476, 1974.

Two pesticides of the carbamate type, Carbaryl (1-naphthyl-N-methylcarbamate) and Arprocarb (2-isopropoxyphenyl-N-methylcarbamate) were tested for neurotoxicologic effects in subacute experiments using male white rats. In the neurotoxicologic examinations mild, but permanent and increasing, functional deviations of the nervous system were found, which could be readily demonstrated by the methods used. Carbaryl caused mild inhibition of the cholinesterase activity in various parts of the brain; the blood cholinesterase activity was practically unchanged. Protein content of the brain parts increased significantly after treatment with both compounds. No alterations were found in body and organ weights, respectively (except that of the adrenals), and no change was observed in the histologic examinations. After exposure of these reversible cholinesterase inhibitors, the presence of a normal value for blood cholinesterase activity does not preclude the possibility of poisoning. 19 references. (Author abstract modified)

188875 Smith, Roger B.; Rossi, Victor; Orzechowski, Raymond F. Department of Pharmacology, Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Interactions of chlorpheniramine ethanol combinations: acute toxicity and antihistaminic activity.** Toxicology and Applied Pharmacology. 28(2):240-247, 1974.

Interactions of chlorpheniramine - ethanol combinations were studied in rats. Significant toxicologic and pharmacologic interactions occurred between chlorpheniramine maleate and 25% v/v ethanol at several dosage combinations. Conditions of both independence and antagonism of acute toxicity were observed in LD50 determinations of chlorpheniramine - ethanol combinations in mice, and confirmed expected results based on the toxicologic pattern of the agents when administered singly. Enhancement of the antihistaminic action of chlorpheniramine by ethanol was demonstrated during histamine - aerosol challenge studies in guinea pigs. 21 references. (Author abstract)

188876 Sofia, R. Duane; Knobloch, Linda C. Department of Pharmacology, Wallace Laboratories, Cranbury, NJ 08512 **Influence on acute pretreatment with delta9-tetrahydrocannabinol**

of the LD50 of various substances that alter neurohumoral transmission. Toxicology and Applied Pharmacology. 28(2):227-234, 1974.

The influence of acute pretreatment with delta9-tetrahydrocannabinol (THC) on the LD50 of various substances that alter neurohumoral transmission was studied. THC significantly influenced the acute lethal effects in mice of several drugs which alter cholinergic, adrenergic and serotoninergic neurotransmission. The LD50 values of carbachol chloride, arecoline HCl, physostigmine salicylate and neostigmine methylsalicylate were all significantly potentiated after pretreatment with THC. Paradoxically, lethality produced by methacholine and exogenously administered acetylcholine were attenuated. Evidence for an alapha-adrenergic receptor blocking effect of THC was noted by the significantly larger LD50 values for l-norepinephrine bitartrate and phenylephrine HCl when each was given in combination with THC. The combination of THC and cyproheptadine HCl was more toxic than the latter compound alone, suggesting an additive antiserotonin effect. 24 references. (Author abstract modified)

189209 Kimishima, Kenjiro; Tanabe, Kyoko; Yamazaki, Michiyo; Takagi, Masanori. Department of Pharmacology, Tottori University School of Medicine, Japan **Investigation of physical dependence on a new benzodiazepine derivative, Bromazepam.** Journal of the Yonago Medical Association (Yonago). 22(5/6):369-375, 1971.

Physical dependence of Wistar rats on bromazepam as compared with diazepam and phenobarbital was studied. Rats treated with bromazepam (10-240mg/kg/day, to a total dose of 3,200mg/kg) showed little bodyweight loss during or after interruption or termination of treatment, while rats treated with phenobarbital (60mg/kg/day for 31 days) showed a significant weight loss after termination of treatment and required 10 days to restore the original bodyweight. The rats previously treated with phenobarbital were treated with bromazepam (120mg/kg/day for 12 days) and showed almost no weight loss after termination of treatment, indicating that there is no mutual dependence between bromazepam and phenobarbital. Weight loss induced by diazepam was between that induced by bromazepam and phenobarbital. 6 references.

189517 Jacob, Joseph J.; Tremblay, Evelyne C.; Colombel, Marie-Claude. Institut Pasteur, 28, rue du Dr. Roux, F-75015 Paris, France **/Enhancement of nociceptive reactions by naloxone in mice and rats./** Facilitation de reactions nociceptives par la naloxone chez la souris et chez le rat. Psychopharmacologia (Berlin). 37(3):217-223, 1974.

The effects of graded doses of naloxone on nociceptive reactions of mice and rats of different strains were studied using a hot plate technique. Enhancements were observed provided the control reaction times were long enough, a condition which was fulfilled for the jumping reaction at different temperatures of the hot plate (50, 55, 65, 80 degress C in mice -- 55 degrees C in rats) but for the licking reaction only at the lowest temperature. Enhancement was dose related up to a ceiling effect. Nalorphine had no such overt action. As low doses of naloxone were effective, the enhancement is most simply accounted for by interactions at the level of the specific opioid receptors, some of which are suggested. The phenomenon might be relevant to the interpretation of the mechanisms of precipitated abstinence. 15 references. (Author abstract)

189564 Sobotka, Thomas J.; Cook, Michelle P.; Brodie, R. E. Division of Toxicology, Food and Drug Administration, Washington, DC **Effects of perinatal exposure to methyl mercury on functional brain development and neurochemistry.** Biological Psychiatry. 8(3):307-320, 1974.

The effects of perinatal exposure to methyl mercury on functional brain development and neurochemistry were examined in rats. Methyl mercury chloride was administered orally to pregnant rats throughout the period of organogenesis (days 6 through 15 of pregnancy). Indices of development were followed throughout the 4 week postnatal period and neurochemical changes were determined in the weanling male offspring. No overt signs of neurotoxicity were noted in either the mothers or pups. Subtle changes were effected in the neonatal sequence of development, involving eye opening and neuromotor coordination, as well as in the neurochemical profile (regional brain pseudocholinesterase activity, serotonin, and norepinephrine) of the 28-day-old weanlings. 23 references. (Author abstract)

189582 Datta, Ranajit K.; Ghosh, Jagat J.; Antopol, William. Department of Pathology, Beth Israel Medical Center, New York, NY 10003 **Mescaline-induced changes of brain cortex ribosomes: effect of mescaline on the binding of amnioacyl-transfer ribonucleic acid to ribosomes of brain tissue.** Biochemical Pharmacology (Oxford). 23(12):1687-1692, 1974.

The effect of mescaline sulfate on the binding of aminoacyl-transfer-ribonucleic acid (t-RNA) by goat brain cortex ribosomes was studied. The poly U directed binding of 14C-phenylalanyl-tRNA in vitro was moderately inhibited by mescaline. The pretreatment of normal ribosomes with mescaline caused a decrease of their phenylalanyl-tRNA binding capacity. The pretreatment of brain cortex slices with mescaline also decreased the phenylalanyl-tRNA binding capacity of the ribosomes isolated from the slices so treated. This was true in assays with phenylalanyl-tRNAs from both Escherichia coli and yeast. This inhibitory effect was dependent on the concentration and length of treatment of brain cortex slices with mescaline. 14 references. (Author abstract)

189583 Proakis, Anthony G.; Borowitz, Joseph L. A. H. Robins Research Laboratories, Richmond, VA **Blockade of insulin release by certain phenothiazines.** Biochemical Pharmacology (Oxford). 23(12):1693 - 1700, 1974.

The blockade of insulin release by phenothiazines is reported in rats. Chlorpromazine lowered the ratio or plasma insulin to blood glucose in adrenalectomized rats fed a glucose load. Desmethylchlopromazine also lowered this ratio 30 min after glucose administration, but elevated it at 60 min. By contrast, fluphenazine had no significant effect on the ratio of plasma insulin to blood glucose. Chlorpromazine and desmethylchlorpromazine were more effective than fluphenazine in blocking insulin release from the isolated rat pancreas. Although adrenal epinephrine release and blockade of the effect of insulin may also be involved, the results of this study show that the hyperglycemic effect of certain phenothiazines is mainly determined by blockade of insulin release. 28 references. (Author abstract)

189587 Clark, W. G.; Vivonia, C. A.; Menon, M. K.; Kurtz, S. M.; Mattis, P. A.; Suzuki, Y.; Page, J. G.; Cotzias, G. C. Psychopharmacology Research Laboratory, VA Hospital, Sepulveda, CA 91343 **The acute toxicity of L-dopa.** Toxicology and Applied Pharmacology. 28(1):1-7, 1974.

The acute toxicities of L-dopa in neonatal and adult rats of both sexes and various strains, in adult mice of both sexes and strains and in rabbits is presented. The ip toxicity values ob-

tained for mice were fairly close except for the results obtained in Spartan Swiss-Webster mice by Parke-Davis. The ip values in RFVL mice obtained by Sankyo compare well with the other data, but their po and sc values are nearly identical, suggesting complete absorption from the intestine. Considerable variation also exists in the data obtained for rats. The po LD50 ranges from 1780-8000mg/kg and the ip LD50 ranges from 624 to 2935mg/kg. The data show that not only are there strain differences, but even different batches of animals of the same strain from the same source and under the same conditions will yield different LD50 values on the same or different days. It is suggested that because of known diurnal circadian rhythms in drug responses, the tests should be carried out at the same time of day and differences due to different excipients also must be taken into account. 9 references.

189588 Rosenkrantz, Harris; Heyman, Irwin A.; Braude, Monique C. Mason Research Institute, Worcester, MA 01608 **Inhalation, parenteral and oral LD50 values of delta9-tetrahydrocannabinol in Fischer rats.** Toxicology and Applied Pharmacology. 28(1):18-27, 1974.

In order to resolve the differences in reported LD50 values for delta9-tetrahydrocannabinol (THC) obtained with various vehicles and rat strains, the oral LD50 values of THC in a natural vegetable oil vehicle and in an aqueous emulsion were determined in the same rat strain. Marihuana cuttings were impregnated with THC and formed into cigarettes which were smoked under controlled conditions of puff volume and duration in an automatic smoking machine to obtain an inhalation LD50. It was demonstrated that behavioral and physiological responses to THC occurred sooner with the oral emulsion formulation than with the vegetable oil. The intragastric LD50 with the emulsion was 800mg/kg and with the sesame oil formulation, 127mg/kg. The iv LD50 was 36-40mg/kg, similar to the inhalation dose when the latter was corrected for THC losses in the rodent nasal passages. The results affirmed that the LD50 values obtained were reliable and that the vehicle did not contribute to the toxicity. 20 references. (Author abstract modified)

189598 Mantilla-Plata, Bernardo; Harbison, Raymond D. Department of Pharmacology, Vanderbilt Medical Center, Nashville, TN 37232 **Effects of phenobarbital and SKF 525A pretreatment, sex, liver injury, and vehicle on delta9-tetrahydrocannabinol toxicity.** Toxicology and Applied Pharmacology. 27(1):123-130, 1974.

The effects of phenobarbital and SKF 525A pretreatment, sex, liver injury, and vehicle on delta9-tetrahydrocannabinol (THC) toxicity were studied. Phenobarbital (PB) antagonizes and SKF 525A potentiates THC induced mortality. PB and SKF 525A alter THC plasma concentrations, distribution, and excretion. SKF 525A pretreatment resulted in a significantly higher plasma and brain 14C concentration. PB pretreatment resulted in a slight reduction of plasma and brain 14C concentration. Neither pretreatment significantly alters the total percent of dose excreted, but both treatments resulted in significantly greater 14C excretion in urine when compared to controls. Male mice are more sensitive to THC induced toxicity than female mice. Presence of liver injury produced a three to five fold increase in THC induced lethality when compared to THC alone. THC suspended in Tween 80 and saline is five times more toxic than the same dosage administered in an oil solution. 17 references. (Author abstract modified)

189600 Drew, Robert T.; Fouts, James R. Pharmacology and Toxicology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC 27709 **The lack of effects of pretreatment with phenobarbital and chlorpromazine on the acute toxicity of benzene in rats.** Toxicology and Applied Pharmacology. 27(1):183-193, 1974.

The lack of effects of pretreatment with phenobarbital and chlorpromazine on the acute toxicity of benzene in rats are reported. The LD50 for animals injected with benzene and the LC50 for animals inhaling benzene were calculated for control groups and those pretreated with either phenobarbital or chlorpromazine. Neither the LD50 or the LC50 were affected by any of the treatment protocols. In order to determine that the pretreatment was stimulating benzene metabolism, a method for measuring benzene metabolism has been developed using 014C0benzene. It is concluded that phenobarbital and 3-MC do induce benzene metabolism in the liver, that chlorpromazine slightly induces benzeme metabolism in the lung, and that pretreatment by these compounds does not affect the acute inhalation toxicity or the ip toxicity of benzene. 11 references. (Author abstract modified)

191123 Loskutova, Z. F.; Saksonov, P. P. Institute of Biophysics, Moscow **/Features of the effect of sympathomimetic amines in radiation affections./** Osobennosti deystviya simpatomimeticheskikh aminov pri radiatsionnykh porazheniyakh. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 76(8):83-85, 1973.

The effect of sympathomimetic amines in irradiated frogs and mice was studied. The toxicity of adrenalin, adrenalon, pervitin, phenamine, veritol, ephedrin, and sympathol was doubled or more in comparison with nonirradiated animals. The action of the amines on the reflex activity of the central nervous system was considerably diminished in the irradiated as compared to the nonirradiated animals. The waking action of phenamin and pervitin on irradiated mice under the influence of hexenal was much less than on nonirradiated mice. In irradiated animals ephedrin even intensified the hypnotic effect of hexenal. (Author abstract modified)

191947 Yunger, Libby M.; McMaster, Scott E.; Harvey, John A. Department of Psychology, University of Iowa, Iowa City, IA 53342 **Neurotoxic effects of p-chloroamphetamine (p-CA) on perikarya of raphe neurons.** Pharmacologist. 16(2):244, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the neurotoxic effects of p-choloramphetamine (p-CA) on perikarya of raphe neurons of rats were reported. Dosages of 10mg/kg produced signs of neuronal toxicity, in Nissl stained sections, which were restricted to perikarya in the raphe nuclei, and detectable by 2 days after injection. The reacting cells showed: cellular shrinkage; dark staining of the cytoplasm; and a perineuronal space. Dosages of 20mg/kg p-CA increased the number of reacting cell bodies in raphe nuclei, and also produced similar reactions in perikarya of substantia nigra. There was no evidence of either terminal degeneration or cellular argyrophilia of raphe neurons in sections stained by the De Olmos and Ingram method, at 2 or 3 days after drug injection. The response of raphe neurons to p-CA resembles the changes seen in substantia nigra after 6-hydroxydopamine. These results indicate that at least some of the raphe neurons are undergoing degenerative reactions to p-CA or a metabolite. (Author abstract modified)

191954 Silbergeld, E. K.; Goldberg, A. M. Johns Hopkins University, Baltimore, MD 21205 **Cholinergic-aminergic interactions in lead-induced hyperactivity.** Pharmacologist. 16(2):249, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, cholinergic - aminergic interactions in lead induced hyperactivity were reported in mice. Chronic low level lead exposure during the suckling period results in a significant increase in motor activity of mice which is suppressed by the amphetamines and methylphenidate. The hyperactivity of lead treated mice is suppressed by cholinergic agonists (oxotremorine, physostigmine and 2-dimethylaminoethanol) and by the aminergic antagonist alpha-methylparatyrosine. In lead treated hyperactive mice, the high affinity transport of dopamine is reduced by 20%, choline by 50%, and tyrosine is increased by 15%. Steady state levels of norepinephrine are increased by 25% while dopamine and acetylcholine levels are unchanged. These results support the concept that cholinergic - aminergic interactions are altered in lead induced hyperactivity. (Author abstract modified)

191957 Michaelson, I. A.; Greenland, R. D.; Roth, W. Department of Environmental Health, University of Cincinnati, Cincinnati, OH 45219 **Increased brain norepinephrine turnover in lead exposed hyperactive rats.** Pharmacologist. 16(2):250, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, it was reported that metabolism of norepinephrine (NE) in brain of developing rats may be affected by exposure to relatively low levels of lead (Pb), leading to increased activity. Steady state levels of brain NE was increased, whereas dopamine (DA) was the same in both control and leaded rats. The turnover of NE appears to be increased in leaded animals whereas DA is essentially unchanged. It may be that exposure to Pb during early brain maturation leads to altered functional activity of those areas of CNS controlling specific functions in which NE and DA serve as neurotransmitters. (Author abstract modified)

191993 Bright, T. P.; Farber, M. G.; Brown, D. J., Forney, R. B. Department of Toxicology, Indiana University Medical Center, Indianapolis, IN 46202 **Cardiopulmonary effects of cannabidiol in anesthetized dogs.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the cardiopulmonary effects of cannabidiol (CBD) were investigated in artificially ventilated, pentobarbital anesthetized dogs. Half of the dogs received CBD suspended in propylene glycol (PG) and half received PG alone. Lung compliance (CL), lung resistance (RL), arterial blood gases (ABG), heartrate (HR), mean systemic blood pressure (BP), and cardiac output (C.O.)were measured before and at 5 min intervals after injection. PG animals showed no significant change in CL, RL, ABG, HR, BP or C.O. All CBD dogs demonstrated a decrease in CL. All CBD dogs had either increased HR or BP or both. In CBD dogs, a transient decrease (5-10%) in C.O. was demonstrated 15 min postinjection. The hypothesis that CBD induced interstitial pulmonary edema, probably via cardiovascular effects is supported. (Author abstract modified)

192013 Blum, Kenneth; Eubanks, Joseph D.; Wallace, Jack E.; Tabor, Robert G. University of Texas Health Sciences Center, San Antonio, TX 78284 **Nonspontaneous convulsions in mice elicited by some catecholamine releasers and 6,7 dihydroxytetrahydroisoquinoline (TIQ)** Pharmacologist. 16(2):307, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of 6,7-dihydroxytetrahydroisoquinoline (TIQ) and amphetamine (AMP) and tyramine (TY), other catecholamine releasing agents, on central nervous system activity were reported. TIQ, AMP, TY and artificial cerebral spinal fluid (CSF) were intracerebrally injected into mice. Convulsions were scored over a 5 hour period. All three catecholamine releasing agents resulted in significantly greater convulsion scores as compared to the CSF control. Pretreatment with alpha methyl-p-tyrosine, a catecholamine synthesis inhibitor, blocked the nonspontaneous convulsions elicited by TIQ, TY and AMP. TIQ induced nonspontaneous convulsions may be due to released catecholamines rather than direct CNS stimulations. (Author abstract modified)

06 METHODS DEVELOPMENT

188228 Barry, Herbert, III. Dept. of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Classification of drugs according to their discriminable effects in rats.** Federation Proceedings. 33(7):1814-1824, 1974.

The classification of drugs by training the animal to make a differential response on the basis of drug condition, using the drug as the discriminative stimulus, is examined. A discriminative response is established by differential reinforcement in a series of training sessions under the drug and nondrug conditions or under two different drugs. Drug conditions with stimulus characteristics resembling one of the training conditions can be identified by consistent choice of one of the alternative responses during tests under novel doses or drugs. These tests of discriminative stimulus properties have identified the following categories of drugs: a) central sedatives, including barbiturates and the 'minor tranquilizers' (chlordiazepoxide and meprobamate); b) central anticholinergics (antimuscarinics); c) nicotine; d) marihuana or its component delta9-tetrahydrocannabinol; e) hallucinogens (mescaline, LSD). Drugs with apparently weaker discriminable effects include 1) chlorpromazine, the 'major tranquilizer', and other phenothiazines; 2) amphetamine; and 3) morphine. The discriminative stimulus seems to be a central drug effect, and the differential response is difficult to establish with peripheral drug effects. The review includes discussion of advantages of this behavioral pharmacology technique and needs for future research. 57 references. (Author abstract modified)

190902 Beckett, A. H.; Essien, E. E.; Smyth, W. Franklin. Pharmacy Department, Chelsea College, University of London, Manresa Road, London S.W.3, England **A polarographic method for the determination of the N-oxide, N-oxide-sulphoxide and sulphoxide metabolites of chlorpromazine.** Journal of Pharmacy and Pharmacology (London). 26(6):399-407, 1974.

Cathode ray polarography was used to measure chlorpromazine-N-oxide, N-oxide sulphoxide and chlorpromazine sulphoxide in mixtures. The response was linear when the metabolites were present in the range 10 micromole to .05 micromole in aqueous solutions. Reductive polarography of the mixed oxides were determined by subtraction. Ultraviolet and potentiometric titration methods were used to determine the pKa values of the oxide metabolites of chlorpromazine. The mechanism of the reduction process was investigated using d.c. polarography and preparative microelectrolysis. Polarographic analysis was applied to the determination of the metabolites after their separation from urine, plasma and microsomal preparations. 13 references. (Author abstract)

191514 Weiner, Norman. University of Colorado School of Medicine, Denver, CO **A critical assessment of methods for the determination of monoamine synthesis and turnover rates in vivo.** Psychopharmacology Bulletin. 10(3):28-29, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in

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December, 1973, steady state and nonsteady state methods for the determination of monoamine synthesis and turnover rates in vivo were assessed. The steady state techniques assume that the system behaves as an open, single, homogeneous compartment, wherein the transmitter is in rapid equilibrium and whose transmitter dynamics obey first order kinetics. In nonsteady state techniques, varying degrees of perturbation of the system are imposed. Because of the delicate servomechanisms which tend to regulate neurotransmitter metabolism in vivo, the nonsteady state methods suffer from inherent theoretical difficulties, since the system being measured may respond in a complex manner when it is disturbed. Turnover studies are of practical usefulness because they provide information about the relative turnover rates of the neurotransmitter under different circumstances. However, studies have shown that steady state techniques also have some basic methodological problems and that it may be injudicious, particularly in brain studies, to assume that the amine pools under examination are present in a simple, homogeneous system which is in rapid equilibrium and which obeys first order kinetics, as has been customary in the past.

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

188501 Yamamoto, Junji. Department of Neuropsychiatry, Osaka University, Medical School, Japan **The effect of a new benzodiazepine derivative nimetazepam on the sleep cycle in man.** Clinical Psychiatry (Tokyo). 15(8):893-897, 1973.

The effect of nimetazepam (Ni) on sleep is studied. An experiment was conducted in which one 23-year-old healthy female and one 24-year-old female with complaints of insomnia and irregular cardiac contraction were treated with Ni, with their EEG being recorded all night. In the female with insomnia, the sleeping pattern after 40 hr. sleep deprivation and that under Ni treatment is almost the same. It is concluded that Ni is a superior hypnotic tranquilizer. In both females, decreases were observed in the time between bedtime and getting to sleep, paradoxical sleep periods, hump - K-complex periods and spindle periods. 18 references.

189059 Resnick, Richard B.; Volavka, Jan; Freedman, Alfred M.; Thomas, Muriel. Department of Psychiatry, New York Medical College, 5 East 102nd Street, New York, NY 10029 **Studies of EN-1639A (Naltrexone): a new narcotic antagonist.** American Journal of Psychiatry. 131(6):646-650, 1974.

The narcotic antagonist EN-1639A (naltrexone) was studied in 37 heroin addicts and found to be clinically useful. There was a low incidence of side-effects, lack of toxicity, high degree of acceptability to the patient, and capacity to antagonize the euphoric effects of heroin for up to 72 hours after a single oral dose. These findings provide a basis for expanding studied of the clinical efficacy of naltrexone in the treatment of opiate dependence. 6 references. (Author abstract)

190146 Brown, Clinton C.; McAllister, Diane R.; Turek, Ibrahim. Biomedical Sciences Division, Maryland Psychiatric Research Center, Baltimore, MD **Psychomotor test performance with a fenfluramine-amphetamine combination.** Journal of Clinical Pharmacology. 14(7):369-376, 1974.

Psychomotor test performance with a fenfluramine-amphetamine combination was examined in 24 normal, nonobese subjects. Subjects performed before drug administration and at 45, 90, 150, and 210 minutes after ingestion. Four treatments used were 10mg dextroamphetamine, 30mg fenfluramine, a combination of the two doses, and a placebo. A double-blind format was employed and all orders of administration were used. Findings reveal significance on six of the ten tests given, usually between dextroamphetamine and placebo. Fenfluramine alone did not significantly differ from placebo on any test. The combination of drugs produced performances similar to that of dextroamphetamine alone. 10 references. (Author abstract modified)

190242 Green, Douglas O.; Reimer, Donald R. Menninger School of Psychiatry, Topeka, KS **The methohexital-methylphenidate interview: a proposed new drug combination for narcotherapy.** Bulletin of the Menninger Clinic. 38(1):76-77, 1974.

A combination of methohexital and methylphenidate for use in narcotherapy is examined. Clinically, the same results have been obtained with the two in combination as with the more traditional 'narcotherapy' drugs: the recovery and abreaction to suppressed and preconscious material. The use of methohexital and methylphenidate enables the therapist to reach these goals in a manner which offers greater control over the interview situation, greater efficiency, and a greater margin of safety for the patient. 4 references.

191777 Myagi, M. A. Department of Neurology and Neurosurgery, Tartu University, Tartu, USSR **/The use of ethymisol (ethylnorantiphein) in patients with prolonged disturbances of consciousness./** Primeneniye etimizola u bol'nykh s dlitel'nymi rasstroystvami soznaniya. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 19-26). Vol. 9.

The effectiveness of Ethymisol or ethylnorantiphein on prolonged disturbances in consciousness was investigated. The effect was found to vary depending on the phase of consciousness restoration. It is concluded that Ethymisol has an analeptic action on automatic, motor, and psychic functions. Ethymisol is indicated in cases of depressed breathing and circulation but contraindicated in cases of tonic extensor spasms, hyperventilation, tachycardia, and hyperthermia. During phases of Appalachian syndrome, akinetic mutism and restoration of verbal contact, Ethymisol can be used to facilitate psychic functions. Ethymisol is recommended to activate focal EEG changes. 10 references. (Author abstract modified)

191790 Myagi, M. A.; Ellamaa, A. N.; Roolayd, E. A. Dept. of Neurology and Neurosurgery, Tartu Univ., Tartu, USSR **/Changes in rhythms of bioelectrical activity of the cerebral cortex in humans under the influence of ethymisol./** Izmeneniya ritmov bioelektricheskoy aktivnosti kory golovnogo mozga cheloveka pod vlinaniyem etimizola. In: Saarma, Yu., Voprosy klinicheskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 167-173). Vol. 9.

The effect of intravenous administration of Ethymisol (Ethylnorantiphein) in a dosage of lmg/kg on the electroencephalogram of healthy humans was studied. The effect of injection passed quickly. The predominant pattern initially was a shift to desynchronization of cortical bioelectrical activity, but the opposite took place in some subjects. After 9-10 minutes, synchronization increased. Ethymisol increased the total integral value of EEG activity; theta wave activity also increased, but beta waves decreased. Alpha activity at first decreased, then increased. Thus Ethymisol has a stimulative effect on the reticular ascending activating system and thalamic and hypothalamic synchronizing structures. 14 references. (Author abstract modified)

192391 Troupin, Allan S.; Green, John R.; Levy, Rene H. Department of Neurological Surgery, University of Washington School of Medicine, Seattle, WA 98195 **Carbamazepine as an anticonvulsant: a pilot study.** Neurology. 24(9):863-869, 1974.

In preparation for a major double-blind, crossover study comparing carbamazepine with diphenylhydantoin (DPH), a pilot study was carried out in 12 patients who had a minimum of four focal or major seizures per month. The dose equivalency between carbamazepine and DPH was found to be 3 to 1, and the study demonstrated an effective method for crossover from one agent to the other. It was determined that the half-life of carbamazepine is in the 12 hour range, so that twice daily doses are effective. At high doses, acute toxicity could be avoided by giving thrice daily doses. In seven of the 12 patients in the pilot study, carbamazepine was the preferable drug. It appears to be an effective independent anticonvulsant

of the same order of magnitude as DPH. 26 references. (Author abstract)

08 DRUG TRIALS IN SCHIZOPHRENIA

187869 Donlon, Patrick T.; Rada, Richard T. Department of Psychiatry, University of California at Davis, 2252 45th Street, Sacramento, CA 95817 **High dosage piperacetazine (Quide R) in ambulatory schizophrenic patients: therapeutic efficacy and toxicity.** Diseases of the Nervous System. 35(5):231-236, 1974.

As the part of a rater blind study the therapeutic efficacy and toxicity of high dosage piperacetazine in ambulatory schizophrenic patients were investigated. A total of 16 patients diagnosed as either chronic undifferentiated or chronic paranoid types served as subjects. They were initially placed on standard dose piperacetazine following a washout period. The dosage was gradually increased until the patient achieved maximum effect with a minimum of side-effects. Two clinical groups (one receiving 25-160mg/day, the other, 160-400mg/day) were compared. High dose piperacetazine was found to be effective in seven patients refractory to low dosage. Although the incidence of side-effects was higher with the high dose patients, toxicity was not increased in patients requiring high dose medication. Indications for high dose neuroleptics are briefly discussed. 17 references. (Author abstract modified)

188115 Kaplan, Jonathan; Dawson, Susan; Vaughan, Thomas; Green, Richard; Wyatt, Richard Jed. Division of Special Mental Health Research, IRP, St. Elizabeths Hospital, WAW Bldg., Washington, DC 20032 **Effect of prolonged chlorpromazine administration on the sleep of chronic schizophrenics.** Archives of General Psychiatry. 31(1):62-66, 1974.

The sleep of 13 chronic male schizophrenics was studied during a 1 month trial of chlorpromazine and compared with 1 month placebo periods. Electroencephalographic recordings were made only after the patients had been on chlorpromazine hydrochloride or a placebo for at least 3 weeks. Sleep latency and awake time were significantly decreased on chlorpromazine while stage II, delta sleep, delta%, nonrapid eye movement (NREM) sleep, REM activity, REM latency, and REM density were significantly increased. There were no significant changes in REM time, REM%, stage II%, and NREM%. 44 references. (Author abstract)

188934 Ito, Yasuyoshi. National Nagoya Hospital, Japan **Clinical experiences with Mesoridazine (TPS-23): its administration to hospitalized schizophrenic patients.** Medical Consultation & New Remedies (Tokyo). 10(8):209-218, 1973.

The effect of mesoridazine (TPS-23) on schizophrenia was studied, based on a clinical administration of TPS-23 (75-400mg/day) for 28-90 days to 30 schizophrenic patients. All the clinical symptoms disappeared and extreme improvement was observed in 12 patients (40.0%), and more than 70% of the clinical symptoms disappeared in 13 patients (43.3%). Good effects were observed in 100% of the patients of paranoid type, 81.8% of those of catatonic type, and 77.8% of those of hebephrenic type. Side-effects, such as dizziness and sense of fatigue were frequently observed, but they were minor and transient. 13 references.

189072 Gallant, Donald M.; Mielke, David H.; Spirtes, Morris A.; Swanson, William C.; Bost, Robert. Tulane University School of Medicine, 1430 Tulane Ave., New Orleans, LA 70112 **Penfluridol: an efficacious long-acting oral antipsychotic compound.** American Journal of Psychiatry. 131(6):699-702, 1974.

A 6 month evaluation of penfluridol, a long-acting oral preparation, was conducted with 50 severely ill schizophrenic patients. After an initial 3 month stabilization period, the patients were divided into two equal groups and a double-blind evaluation of penfluridol versus placebo was conducted. The results indicated that weekly administration of penfluridol provides relatively safe and adequate control of severely ill schizophrenic patients and displays efficacy similar to that of the shorter acting antipsychotic agents. 6 references. (Author abstract modified)

189095 Donlon, Patrick T.; Tupin, Joe P. Department of Psychiatry, University of California at Davis, 2252 45th St., Sacramento, CA 95817 **Rapid 'digitalization' of decompensated schizophrenic patients with antipsychotic agents.** American Journal of Psychiatry. 131(3):310-312, 1974.

A method of administering high dosages of the more potent, less sedating antipsychotic drugs to schizophrenic patients to promote the patients' rapid improvement is described. This method has been effective in keeping the periods of hospitalization of more than 150 schizophrenic patients brief, and the patients have been managed in an open ward community setting. 9 references. (Author abstract modified)

190239 Adams, Ralph N. Chemistry Dept. University of Kansas, Lawrence, KS **An overview of the 6-hydroxydopamine theory of schizophrenia.** Bulletin of the Menninger Clinic. 38(1):57-69, 1974.

The history and background of the 6-hydroxydopamine (6-OHDA) theory of schizophrenia are discussed, and merits and shortcomings of the theory are examined. The principal dysfunctions underlying schizophrenia are seen as a lack of goal directed or reward seeking behavior. Injections of 6-OHDA depressed a variety of consumptive behaviors. Chlorpromazine eliminated the effects of injected 6-OHDA on self-stimulation rates. 28 references.

191044 Ayd, Frank J., Jr. no address **The future of pharmacotherapy: new drug delivery systems.** Baltimore, International Drug Therapy Newsletter, 1973. 115 p. $6.00.

The probable future trend in the treatment of chronic schizophrenia, which involves to a large extent the use of prolonged action drugs, especially the depot preparations, is discussed. The major drugs in question are fluphenazine enanthate and fluphenazine decanoate, the first two depot neuroleptics that have had extensive trial. Clinical experiences and the chemical and pharmacological backgrounds of this treatment approach are reported and indications and contraindications, adverse reactions and their management are examined. The ambulatory treatment of those chronic patients who need maintenance therapy and who will not take drugs in a regular and reliable fashion is emphasized. Advantages other than control of drug deviations include the fact that aggregate dosage per month is far lower with injectables and that the patient is freed from a continuous routine of drug taking. A lesser advantage is that the injection of depot drugs is somewhat less costly than oral medication in terms of personnel time and in terms of reduced dosage. The method for administering the drugs is also described.

191290 Snyder, Solomon H.; Banerjee, Shailesh P.; Yamamura, Henry I.; Greenberg, David. Dept. of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Drugs, neurotransmitters, and schizophrenia.** Science. 184(4143):1243-1253, 1974.

Of various biochemical approaches to the study of schizophrenia, the investigation of brain neurotransmitter interactions with psychotropic drugs has proved most productive. Analyses of the mechanism of the antischizophrenic activities of the phenothiazines and the ability of amphetamines to worsen schizophrenic symptoms and elicit a schizophrenia like psychosis have focused attention upon dopamine in the brain. An enzymatic activity that utilizes the methyl group of 5-methyltetrayhdrofolic acid to O-methylate and N-methylate phenylethylamines and indoleamines, thereby forming psychotomimetic drugs, is a possible mechanism for the production of such compounds in the mammalian brain. None of these approaches affords the definitive answer and roles for other neurotransmitters, such as acetylcholine and gamma-aminobutyric acid are possible. 84 references.

191320 Bender, D. A.; Bamji, A. N. Courtauld Institute of Biochemistry, Middlesex Hospital Medical School, London W1P 5 PR, England **Serum tryptophan binding in chlorpromazine-treated chronic schizophrenics.** Journal of Neurochemistry (Oxford). 22(5):805-809, 1974.

In a study of serum tryptophan binding, 10 hospitalized chronic schizophrenics receiving large doses of chlorpromazine and orphenadrine were evaluated. In schizophrenics the total serum tryptophan was 50% of normal. The level of diffusible tryptophan (that fraction directly available for uptake into the brain and other tissues) did not suffer so great a reduction, because the number of sites available for tryptophan binding per mole of serum albumin was only half that normally found, although the apparent affinity of the albumin for tryptophan was approximately normal. There was thus a considerable difference in the ratio of diffusible/bound serum tryptophan between the normal and schizophrenic subjects. Reduced serum albumin and elevated serum nonesterified fatty acid levels in the schizophrenics do not appear to account for the abnormality of binding. 15 references. (Author abstract modified)

191508 Janowski, David S.; Davis, John M.; El-Yousef, M. K. University of California School of Medicine, La Jolla, CA **Effects of intravenous d-amphetamine, l-amphetamine and methylphenidate in schizophrenics.** Psychopharmacology Bulletin. 10(3):15-24, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the effects of intravenous d-amphetamine, l-amphetamine, and methylphenidate on the schizophrenic process were reported. Equimolar doses were administered to the patients, and results indicate that methylphenidate is a more potent activator of psychotic behavior than l-amphetamine. If a ratio of effectiveness of 2:1 between d-amphetamine and l-amphetamine represents a dopaminergic phenomenon, it would seem that the general and psychosis activating effects of the two drugs represent a dopaminergic, rather than a noradrenergic phenomenon. Other studies have shown that oral L-dopa also produces a worsening of schizophrenic symptoms. These findings suggest that dopamine may play a role in the schizophrenic process. 18 references.

191593 Ikutomi, Hiroshi; Kimura, Kinichiro. Kokuho Hashimoto Municipal Hospital, Japan **Experiment with Penfluridol (TLP-607) on the treatment of chronic schizophrenia.** Medical Consultation and New Remedies (Tokyo). 11(2):181-189, 1974.

The effect of penfluridol (TLP) on chronic schizophrenia was studied in 13 patients treated with TLP in varying doses over 10-19 weeks, with or without accompanying medication. Schizophrenic symptoms were improved in 45% of the sample, while hallucination and delusion decreased in 40% of the Ss. The most effective dose was 40mg-50mg a week. The drug had no effect on autism and volition. Insomnia and parkinsonian side-effects were frequent and were controlled by accessory medicines. 10 references.

191686 Takemura, Norio; Tanaka, Keiya; Hironaka, Tadao; Sawa, Atsushi; Hamada, Hidehaku. Gunma Hospital, Gunma, Japan **Use of haloperidol (Brotopon) in the treatment of schizophrenia.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(5):653-660, 1973.

The effect of haloperidol on schizophrenia was tested in 47 acute, chronic, and catatonic schizophrenics. The drug was administered orally for 3 months. Haloperidol had its best effect on acute symptoms, with some therapeutic effect on chronic patients, and little or no effect on catatonics. Haloperidol showed marked relief of psychomotor excitation, anxiety and acute abnormal experience. Hallucinations and delusions were controlled to some extent. Extrapyramidal syndrome was the most commonly observed side-effect, and this was controlled by either promethazine or trihexyphenidyl. 14 references.

191720 Ito, Yohiko; Osawa, Shuji. Osaka City Univeristy, Japan **Clinical use of Luvatren (methylperidol) for the treatment of schizophrenia.** Medical Consulation and New Remedies (Tokyo). 11(5):167-176, 1974.

The effectiveness of luvatren (methylperidol) in schizophrenia was assessed in a population of long-term schizophrenics undergoing up to 18 months treatment with this drug. In patients under luvatren treatment alone there was a 57% improvement rate, with 10% terminating due to adverse side-effects. Luvatren shows most promise when used in combination with other drugs. Luvatren and promethazine produced a 63% improvement rate in this population. 21 references.

192431 Van Lommel, R.; Dom, R.; Baro, F. Psychiatric Clinic of the University of Leuven, Belguim **Interaction between neuroleptic therapy and sociotherapeutic approach. An investigation with penfluridol and haloperidol.** Activitas Nervosa Superior (Praha). 16(1):75-76, 1974.

Patients treated with penfluridol were tested for more active adaptation than patients treated with haloperidol. General behavior observations give support to the hypothesis that, with penfluridol in a sociotherapeutic approach, more active adaptation can be obtained than with haloperidol. Patients who become more symptom free and who improve in social adequacy gain on intelligence test scores. In this respect, haloperidol appears to be superior and its effect is additive to that of sociotherapy. 16 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

187477 Vahia, N. S.; Vahia, Vihang. no address **Lithium carbonate in manic depressive psychosis.** Clinician (Goa). 36(1):21-23, 1972.

The effect of lithium carbonate on manic-depressive psychosis was investigated. In selected cases that were likely to be under constant supervision, lithium carbonate was administered in 400-1800mg doses daily. It was concluded that although potentially toxic, lithium is a very useful drug in the

treatment of mania. Absence of side-effects as obtained with the use of phenothiazines makes the drug a drug of choice in the treatment of active, energetic hard working people, because the drug does not entail absence from work. There is no drowsiness or groggy feeling as with phenothiazines. The patients' subjective impression was that the improvement with this drug was better than improvement in the past. Chlorpromazine should be combined with lithium with great caution, but minor tranquilizers can be administered with comparative safety. 6 references.

187536 Ayuso Gutierrez, Jose Luis; Lopez-Ibor Alino, Juan Jose; Montejo Iglesias, Leonor. no address /**Tryptophan and amitriptyline in the treatment of depressions.**/ Triptofano y amitriptilina en el tratamiento de la depresion. Actas Luso-espanolas de Neurologia, Psiquiatria y Ciencias Af. (Madrid). 1(3):471-476, 1973.

The results of a comparative study made of double-blind trial of amitriptyline and l-tryptophan on 30 hospitalized patients suffering from depressive disorders are described and tabulated. All consecutive admissions presenting various forms of depression were included, except those cases that had received electroconvulsive treatment during the preceding month or psychopharmaceuticals during the 15 days prior to the study. Patients over 65 years of age were excluded to reduce the possibility of organic factors due to age. Evaluation was carried out independently by two clinics. Patients who received the amino acid together with amitriptyline were found to improve more than control patients given amitriptyline alone. The average scores obtained on a depression inventory were not significantly different, either at 15 days, or after treatment. There was no evidence that either treatment had any advantage with regard to speed of action. Side-effects were more numerous in patients treated with amitriptyline plus l-tryptophan than control patients, the difference being significant. 7 references.

187839 Maletzky, Barry M.; Klotter, James. U. S. Lyster Army Hospital, Fort Rucker, AL 36360 **Episodic dyscontrol: a controlled replication.** Diseases of the Nervous System. 35(4):175-179, 1974.

Research on the syndrome of episodic dyscontrol and successful treatment of a majority of patients with diphenylhydantoin (Dilantin) is described. A controlled replication of this orginal research employing sequential analysis in a double-blind discontinuation trial is examined. Results indicate a clear superiority for Dilantin over placebo when both are added to a psychotherapeutic treatment regimen for violent behavior. Conclusions based on these results are discussed and suggestions for further research offered. 16 references. (Author abstract modified)

188107 Weckowicz, T. E.; Nutter, R.; Gibbs, J. T. Dept. of Psychiatry, University of Alberta, Edmonton, Alberta, Canada T6G 2G3 **The effect of tranylcypromine (Parnate) on eyelid conditioning and paired associate learning in depressed patients.** Pavlovian Journal of Biological Science. 9(2):122-123, 1974.

The effect of tranylcypromine, a monoamino oxidase inhibitor antidepressant energizing drug, on the level of drive in depressed patients was assessed hypothesizing that if tranylcypromine increased drive it would facilitate eyelid conditioning and paired-associate learning and increase the level of arousal as measured by heartrate, skin conductance, and a response to standard stressor. The 40 Ss were split equally into experimental and control (placebo) groups. All self-rated themselves for depression and were rated by two psychiatrists. Rating procedures are described. All were subsequently eyelid conditioned under constant physiologic monitoring. No significant differences in condition were noted after experimentation in either group on any measure save for a positive association between anxiety scores and both eyelid conditionability and paired-associate learning noted in the placebo group only. Both groups showed clinical improvement. The paradoxical findings suggest that anxiety in tranylcypromine Ss has a disorganizing effect on conditioning and simple learning. The stimulant effect theory of tranylcypromine was not supported and the claim that tranylcypromine has quick action effect is disputed. 6 references.

188348 Mountjoy, C. Q.; Weller, M.; Hall, R.; Price, J. S.; Hunter, P.; Dewar, J. H. Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, England **A double-blind crossover sequential trial of oral thyrotrophin-releasing hormone in depression.** Lancet (London). 1(7864):958-960, 1974.

In a double-blind, crossover, sequential trial, oral thyrotrophin releasing hormone (T.R.H.)(40mg) given daily for a week was no more effective than placebo in treating 29 depressed outpatients. There was no clinical or biochemical evidence that patients continuing on oral T.R.H. (40mg daily) maintenance therapy after completion of the trial became hyperthyroid, even when T.R.H. was administered for 12 weeks. 12 references. (Author abstract)

188517 Nishiura, Nobuhiro, Kuroda, Yoshihiro; Iida, Norihiko; Iwamoto, Nobuyasu Department of Psychiatry, Osaka Medical College, Japan **A case of a non-specific mental illness with psychomotor variant.** Clinical Electroencephalography (Osaka). 15(6):395-396, 1973.

A case of atypical psychosis with psychomotor variant is discussed. A 47-year-old female with no major amnesia began to experience auditory hallucinations and exhibit violent behavior. The content of her hallucination was closely related to her real life and her reaction to it varied. She was treated with haloperidol and other psychotropic drugs during 50 days of hospitalization, and hallucination disappeared. When the patient experienced frequent hallucination, her EEG showed diffuse theta waves of 5 Hz and rhythmic psychomotor variants of 5 HZ for 30 seconds after 2 minute hyperventilation. After the hallucination disappered, no EEG abnormality was observed.

188832 Kragh-Sorensen, Per; Hansen, Christian Eggert; Larsen, Niels-Erik; Naestoft, Jorgen; Hvidberg, Eigill F. Department O, State Mental Hospital, Glostrup, DK-2600 Glostrup, Denmark **Long-term treatment of endogenous depression with nortriptyline with control of plasma levels.** Psychological Medicine (London). 4(2):174-180, 1974.

The clinical pharmacological basis for a correct design of controlled trials of the prophylactic effect of tricyclic antidepressants was examined in depressed patients. Twenty two patients, successfully treated with nortriptyline (NT) in hospital for endogenous depression, continued the treatment for up to 5 months in the outpatient clinic. Plasma levels of NT were checked, and ratings were performed regularly. Depressive relapses, all related to low plasma levels of NT, were seen in three patients. The gas chromatographic method has proved suitable for clinical routine and the results demonstrate the value of monitoring plasma levels in achieving therapeutic control. 29 references. (Author abstract)

188893 Mori, Atsuyoshi; Kunigi, Toru. Toho University School of Medicine, Japan **Clinical experiences with a new anti-**

depressant, maprotiline. Medical Consultation & New Remedies (Tokyo). 10(8):195-200, 1973.

The effect of maprotiline on depression is studied, based on a clinical administration of the drug orally for 1-11 weeks to 20 patients with depression. The drug induced complete remission of the symptoms in 6 patients, almost complete remission in 5, partial remission in 6, and induced no change in 3. The drug was most effective on circulatory depression, and less effective for reactive and volutional depression. Good effects appeared in 9 patients during the first week of administration and in 5 patients during the second week. Side-effects, such as a dry mouth, dizziness, vertigo, drowsiness and tachycardia, were observed in 14 patients; decreased blood pressure was also observed in 2 patients. 3 references.

189076 Ehrensing, Rudolph H.; Kastin, Abba J.; Schalch, Don S.; Friesen, Henry G.; Vargas, J. Rodolfo; Schally, Andrew V. Ochsner Clinic, 1514 Jefferson Highway, New Orleans, LA 70121 **Affective state and thyrotropin and prolactin responses after repeated injections of thyrotropin-releasing hormone in depressed patients.** American Journal of Psychiatry. 131(6):714-718, 1974.

The effectiveness of thyrotropin releasing hormone therapy in depressed patients was studied. Eight patients with serious depression were given 1000mg of thyrotropin releasing hormone (TRH) or saline intravenously for 3 days in a double-blind study. All patients then received 1000mg of TRH daily for the next 7 days. The group receiving saline showed the greatest improvement; only one patient improved substantially while receiving TRH. Plasma thyrotropin and prolactin responses to TRH were distinctly diminished in three of the most severely depressed patients. In depression, the primary value of TRH may be as a diagnostic tool in differentiating among various types of depression. 18 references. (Author abstract modified)

189650 Davis, John M.; Janowsky, David S. University of Chicago, Chicago, IL **Recent advances in the treatment of depression.** British Journal of Hospital Medicine (London). 11(2):219-220, 222, 225-228, 1974.

Problems with the use of two classes of antidepressant drugs, the imipramine type (tricyclic antidepressants) and the monoamine oxidase inhibitors (MAOIs) were investigated. Clinical effects of the drugs are described, based on several studies. It is concluded that the tricyclic antidepressants are probably slightly more effective and slightly safer than MAOIs in the treatment of depression, and that phenothiazine derivatives may also be of value in selected cases, especially where anxiety or agitation are a component of the depressive syndrome. 49 references.

189735 Prien, Robert F.; Caffey, Eugene M., Jr.; Klett, C. James. Central NP Research Laboratory, VA Hospital, Perry Point, MD 21902 **Prophylactic efficacy of lithium carbonate in manic-depressive illness: report of the Veterans Administration and National Institute of Mental Health Collaborative Study Group.** Archives of General Psychiatry. 28(3):337-341, 1973.

In an 18 hospital study, 205 patients hospitalized with a diagnosis of manic-depressive illness, manic type, were treated upon discharge with lithium carbonate or placebo for a 2 year period. Lithium carbonate was significantly more effective than placebo in preventing relapses (i.e.,affective episodes severe enough to require hospitalization or use of nonstudy drugs). The difference in treatment outcome between lithium carbonate and placebo was due mainly to the lower incidence of manic relapses on lithium carbonate. Patients on lithium carbonate also had a lower incidence of depressive relapses than patients on placebo but the limited incidence of severe depression in this sample makes it difficult to draw any conclusions regarding the prophylactic efficacy of lithium carbonate in depressive illness. The results from this trial coupled with those from other studies indicate that lithium carbonate combined with regular clinical appraisals is a safe and effective treatment for preventing relapse in manic-depressive illness. 16 references. (Author abstract)

189775 Flemenbaum, Abraham. Texas Tech University Medical School, Lubbock, TX 79411 **Affective disorders and 'chemical dependence': lithium for alcohol and drug addiction?** Diseases of the Nervous System. 35(6):281-285, 1974.

A working hypothesis for the treatment of some types of 'chemical dependence' on drugs and alcohol, is presented, asserting that in some cases sociopathy, drug abuse, and more specifically, alcoholism, are not single disease entities, but syndromes. Literature suggests that some types of alcoholism may be genetically related to affective disorders and that alcoholism and other related disorders could be 'parapsychiatric' manifestation of subpsychotic mood swings. Increased evidence exists that selected cases of depressive disorders respond to prophylactic administration of lithium carbonate and that lithium seems beneficial in disorders other than affective ones. It is suggested that lithium could be useful in the prophylaxis of these types of parapsychiatric disorders. The characteristics of the syndrome are described. 36 references. (Author abstract modified)

189793 Johnson, Gordon. Department of Psychiatry, New York University School of Medicine, New York, NY **Antidepressant effect of lithium.** Comprehensive Psychiatry. 15(1):43-47, 1974.

Data are presented on a single-blind evaluation of the effectiveness of lithium carbonate treatment in the acute depressive phase. Although the efficacy of the drug was generally demonstrated, the findings must be interpreted cautiously, despite the fact that the patients were all moderately to severely depressed, had been unresponsive to other treatment interventions, and had shown no response to hospitalization and placebo administration prior to lithium treatment. It is suggested that the symptom reduction seen with lithium was unlikely to be the result of nonspecific factors associated with hospital milieu and treatment intervention; that unipolar depressed persons whose characteristics resemble those of endogenous type patient seem responsive to lithium. However, the possibility that lithium may be effective against both acute depression and mania, as well as possess prophylactic efficacy against bipolar recurrences, is difficult to reconcile with any theory that relates bipolarity to change in central biogenic amines in mania and depression. Such data do suggest that this ion may act in normalizing the underlying disorder, rather than merely represent symptoms of a particular phase, making lithium unique among the psychoactive drugs and supporting a theoretical model of manic-depressive illness as continuum phases of the same disorder. 15 references.

190195 Brauzer, B.; Goldstein, B. J.; Steinbook, R. M.; Jacobson, A. F. Department of Psychiatry, University of Miami, School of Medicine, P.O. Box 875, Biscayne Annex, Miami, FL 33152 **The treatment of mixed anxiety and depression with loxapine: a controlled comparative study.** Journal of Clinical Pharmacology. 14(8&9):455-463, 1974.

The therapeutic effects of loxapine succinate were compared with those of chlordiazepoxide and placebo in 115 outpatients exhibiting mild or moderate symptoms of anxiety and depression. They were treated for 4 weeks in a double-blind fashion using a flexible dose range of 4 to 20mg loxapine or 20 to 100mg chlordiazepoxide. Average therapeutic dosages for loxapine and chlordiazepoxide were 7.4mg and 39.4mg, respectively. Loxapine succinate and chlordiazepoxide are more effective than placebo in the treatement of mixed anxiety and depression. There also appears to be differential activity in terms of symptom relief and production of side-effects. 13 references. (Author abstract modified)

190196 Charalampous, K. D.; Freemesser, G. F.; Smalling, Kathryn Ford. Department of Psychiatry, Baylor College of Medicine, Houston, TX **A double-blind controlled study of loxapine succinate in the treatment of anxiety neuroses.** Journal of Clinical Pharmacology. 14(8&9):464-469, 1974.

Loxapine succinate was compared to doxepin and placebo in a double-blind study of 60 outpatients with anxiety neuroses. Clinical evaluations, including the Brief Psychiatric Rating Scale and others, showed no significant differences in improvement among the three groups over the 4 weeks of treatment. Thirty four patients experienced side-effects, mostly mild to moderate. Only one patient was removed from the study because of side-effects. Laboratory evaluations and physiological signs throughout treatment revealed no treatment related abnormalities. It is suggested that in a population of patients with anxiety many nonspecific variables are confounded with the main treatment variable studied. Larger sample sizes may therefore by necessary to distinguish differences due only to pharmacotherapy. 18 references. (Author abstract modified)

190241 Obourn, Robert. Inpatient Service, C. F. Menninger Memorial Hospital, Topeka, KS **A few remarks on the use of psychoactive agents in the treatment of emotional disorders.** Bulletin of the Menninger Clinic. 38(1):72-75, 1974.

The importance of psychoactive drugs for treating emotional disorders is examined. Drug therapy is considered most effective when used in conjunction with psychotherapy. Important aspects of drug therapy are prescribing the correct drug, in the correct amounts, at the correct time, and observing the results, both expected and unexpected. 13 references.

190379 Pineda, Mario R.; Russell, Stanley C. 301 Medical Towers, 440 East Woodrow Wilson Drive, Jackson, MI 39216 **The use of a tricyclic antidepressant in epilepsy.** Diseases of the Nervous System. 35(7):322-323, 1974.

A case report of a patient with a seizure disorder was examined as the seizure frequency increased concomitantly with severe depression. When the seizures failed to respond to the usual management, Desipramin was added to the treatment and, was not only effective in improving the depressive symptoms, but it appeared to contribute to a rather dramatic decrease in the number of seizures being suffered by the patient. 10 references. (Author abstract modified)

190381 Pokorny, Alex D.; Prien, Robert F. Psychiatry Service, VA Hospital, Houston, TX **Lithium in treatment and prevention of affective disorder: a VA-NIMH collaborative study.** Diseases of the Nervous System. 35(7):327-333, 1974.

An evaluation of the use of lithium in treatment and prevention of affective disorders is presented through examination of over 500 patients. Lithium's effectiveness was compared with placebo in preventing recurrence of affective episodes in manic patients. Lithium carbonate, with regular clinical appraisals appears to be a safe and effective treatment for preventing affective episodes in both unipolar and bipolar illness. 10 references.

191026 Gram, Lars F.; Overo, Kerstin Fredricson; Kirk, Lars. Psychochemistry Institute, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark **Influence of neuroleptics and benzodiazepines on metabolism of tricyclic antidepressants in man.** American Journal of Psychiatry. 131(8):863-866, 1974.

The pharmacokinetic interaction between benzodiazepines and nortriptyline were tested in five schizophrenic patients. Each patient was tested during periods of treatment with neuroleptics, diazepam and chlordiazepoxide, and in a drug free control period. Neuroleptics (haloperidol and perphenazine) caused changes indicating inhibition of metabolism of 14C-nortriptyline. Neither of the two benzodiazepines caused a significant change in the pharmacokinetic measurements of 14C-nortriptyline. In rats, the matabolism of 14C-nortriptyline was inhibited by pretreatment with chlordiazepoxide, but only when given in a dose of 60mg/kg a short time before the administration of 14C-nortripyline. 46 references. (Journal abstract modified)

191119 Ayd, Frank J., Jr.; Taylor, Irving J. no address **Thirty-five years' continuous treatment for recurrent depression: from ECT to drugs.** Journal - National Association of Private Psychiatric Hospitals. 6(1):32-35, 1974.

The case history of a unipolar manic-depressive whose illness began in 1938 is described. He was one of the first patients in the world to be treated with electroconvulsive therapy (ECT) and most probably was the first American to be so treated. Between 1938 and 1958, he had 21 episodes of melancholia. For each attack he received an average of 10 ECTs as an inpatient or as an outpatient. Thereafter, for subsequent depressions he received imipramine plus ECT followed by maintenance imipramine therapy for 10 years. Imipramine was discontinued because he developed arteriosclerotic heart disease and later diabetes and peripheral vascular insufficiency. Since 1968 he has been treated with doxepin or doxepin plus tranylcypromine. His clinical course and response to treatment are described. 11 references. (Author abstract modified)

191530 Davis, John M.; Janowsky, David. University of California, San Diego, CA **Cholinergic and adrenergic balance in mania and schizophrenia.** Psychopharmacology Bulletin. 10(3):49-50, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the hypothesis was presented that abnormal behavior, such as that observed in depression, mania and schizophrenia, is under control of more than one transmitter and possibly involves a balance of two or three transmitters. Clinical data were presented indicating that increasing acetylcholine levels with physostigmine reverses some of the symptoms of mania and increases depression in patients with affective disorders. Data were also included to support the suggestion that schizophrenia may be caused in part by dopaminergic overactivity of a yet unspecified source. The possibility that cholinergic factors may play a more predominant role in the control of mania than in schizophrenia was also raised and supported by test data.

191531 Shopsin, Baron; Janowsky, David; Davis, John; Gershon, Samuel. Department of Psychiatry, Neuropsychopharmacology Research Unit, New York University Medical Center, New York, NY **Rebound phenomenon in manic patients following physostigmine: towards an understanding of aminergic mechanisms underlying affective disorders.** Psychopharmacology Bulletin. 10(3):50-51, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a report was presented of a test of the rebound phenomenon observed in physostigmine treated patients. Physostigmine was administered intravenously to three male psychiatric inpatients in the acute manic phase of cyclic manic-depressive illness. All three patients, irrespective of overall dosage, tended to show two distinctive phases, as well as a third postdrug phase referred to as rebounding or compensatory phenomena. Clearcut changes in clinical state occurred 2 hr after the last physostigmine injection. The rebounding phenomena were transient in nature; they are stressed as a clinical index with which to characterize chemically the initial state of amine imbalance responsible for a given affective illness. The data are consistent with an adrenergic - dopaminergic - cholinergic balance hypothesis of affective disorders and may provide a relevant link in understanding the interface or crossover between manic and schizoaffective illness.

191532 Carroll, Bernard J. Mental Health Research Institute, University of Michigan, Ann Arbor, MI **Role of acetylcholine and dopamine in manic behavior.** Psychopharmacology Bulletin. 10(3):51-52, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, five physostigmine tests with four manic patients, testing the role of acetylcholine and dopamine in manic behavior were reported. Findings indicate that the manic thought disorder has a mechanism different from that of the manic psychomotor disorder. The thought disorder was not modified by physostigmine except that it was less obvious due to the overall anergic state. The apparent antimanic effect of physostigmine may be analogous to the apparent antidepressant effect of levodopa. The Janowsky-Davis hypothesis of acetylcholine - dopamine balance in mania, which suggests that central anticholinergic drugs should increase manic behavior, was not supported by data from patients given atropine prior to electroconvulsive shock therapy. Data were also briefly presented on the effects of drugs on a new animal model of mania (stereotyped activation of mice by morphine). Dopamine receptor blockers and synthesis inhibitors antagonized the model behavior; scopolamine and atropine caused potentiation at low doses but antagonism at high doses; and physostigmine had no effect at 0.1mg/kg but caused potentiation at 0.5mg/kg. 1 reference.

191534 Prange, Arthur J., Jr.; Lipton, Morris A.; Wilson, Ian C. Biological Sciences Research Center, University of North Carolina, Chapel Hill, NC **Clinical intimations of amine balance and permission.** Psychopharmacology Bulletin. 10(3):53-54, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, an investigation of the relationships between brain biogenic amines and affective disorders and two types of movement disorders, Parkinson's disease and tardive dyskinesia, was reported. An indoleaminergic predominance may exist in Parkinson's disease and a catecholaminergic predominance in tardive dyskinesia. While L-DOPA is beneficial in Parkinson's disease, excessive amounts may cause a dyskinetic syndrome that resembles dyskinesia. It was hypothesized, therefore, that in tardive dyskinesia there exists a catecholaminergic predominance. In a single-blind crossover study of two patients, lithium carbonate appeared effective as a treatment, and this finding was confirmed by those from other research. It was hypothesized that in the affective disorders, a deficit in central indoleaminergic transmission permits affective disorder but is insufficient for its cause; changes in central catecholaminergic transmission, when they occur in the context of a deficit in indoleaminergic transmission, act as a proximate cause for the disorders and determine their quality, since catecholaminergic transmission is elevated in mania and diminished in depression. 26 references.

191663 Maeda, Susumu. Gunma University School of Medicine, Japan **Treatment of exogenous psychosis by the use of FK-880 (sulpiride).** Medical Consultation and New Remedies (Tokyo). 10(12):155-168, 1973.

The study of sulpiride (FK-800) on exogenous depression was studied in a sample of 37 Ss exhibiting toxic psychosis, symptomatic psychosis, involutional psychosis, organic psychosis, epileptic psychosis, hypochondriasis and hysterical blindness. Ss were treated with sulpiride orally or intramuscularly for as long as 2 years. Sulpiride showed a therapeutic effect in 60% of the patient sample. Sulpiride was particularly effective in toxic psychosis, involutional psychosis, and symptomatic psychosis. Sulpiride was also of value in controlling hallucination, delusion, confusion, and depression. Other useful therapeutic effects are discussed. Side-effects were at a low and acceptable level. 12 references.

191665 Yamashita, Itaru. Hokkaido University, Japan **Experiment with Lopramine (DB-2182) on the treatment of depression.** Medical Consultation and New Remedies (Tokyo). 11(1):235-241, 1974.

The effect of lopramine (DB-2182) on depression was studied, based on an experiment in which 25 patients with psychogenic, endogenous and neurotic depression were treated with lopramine (30-150mg a day) for 6-130 days with or without diazepam and sleeping pills. Lopramine produced some favorable change in 90% of the patient sample. While lopramine seems less effective in controlling depression than imipramine or amitryptyline, it also produces less severe side-effects. 2 references.

191670 Sarai, Keisuke; Kodama, Hisashi; Nomura, Shotaro; Jitsuichi, Shozo; Ishizu, Hiroshi; Amamoto, Takashi; Segawa, Yoshihisa; Masuda, Katsuyuki. Department of Neuropsychiatry, Hiroshima University, Japan **Experiment with lithium carbonate on the treatment of manic state.** Medical Consultation and New Remedies (Tokyo). 11(1):225-232, 1974.

The effect of lithium carbonate (Li) on manic state was studied, based on an experiment in which 30 patients in the manic state were treated with Li (300-1,800mg/day) for 1-28 months with or without accompanying drugs, such as chlorpromazine, haloperidol, levomepromazine, diazepam, and sleeping pills. Li completely eliminated manic state in 18 patients and partially reduced it in 7 others, thus Li was effective in 83.3% of the patients. The effect appeared within 3-14 days after the beginning of Li treatment. Li was most effective for aggression, excitation, and quick temper, and secondarily effective for euphoria, hyperactivity, talkativeness and compulsion for work. Side-effects were generally not critical and Li treatment showed good clinical effect even in small blood levels. Li was

of limited value in controlling the depressive state of manic-depressives. 36 references.

191716 Okada, Michio; Takei, Hiroshi; Mori, Atsuyoshi; Kurokawa, Eizo; Noguchi, Takuro. Kanto Teishin Hospital, Japan **Clinical effects of imipramine-N-oxide on depression.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(12):1447-1456, 1973.

The effect of imipramine-N-oxide on depression was studied in 56 patients with depression or in depressive states treated with this drug (50-150 mg/day) for 6 weeks with or without other drugs. The rate of improvement was 55.4%. This drug was effective on elimination of hypochondriac complaints and inhibition. Side-effects, such as dry mouth, fatigue and manic state, were observed in 31 patients. These side-effects were minor and disappeared immediately after termination of treatment. 13 references.

191723 Tominaga, Hajime; Ishida, Motoo. National Tokyo Daiichi Hospital, Japan **Emergency treatment of an acute state of mental aberration.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(11):1229-1235, 1973.

Emergency treatment of patients with acute mental aberration is discussed. Speed is of utmost importance to prevent the patient from hurting himself or others. Information about the patient should be gathered as quickly as possible by the psychiatrist from family members. Amobarbital sodium and atropine sulfate are the drug combination of choice, and when administered intramuscularly will put the patient to sleep in short order. The physician must be careful to note the occurrence of liver disturbance, blood stream disorder or sensitivity to barbiturates which may complicate this form of therapy. 6 references.

191857 Morris, Jeffery B.; Beck, Aaron T. Hahnemann Hospital, Philadelphia, PA **The efficacy of antidepressant drugs: a review of research (1958 to 1972).** Archives of General Psychiatry. 30(5):667-674, 1974.

An extensive review of published research on the efficacy of antidepressant medications is presented. To overcome the inconsistencies of previous reviews, 146 double-blind studies on medications actively promoted in the U.S. as antidepressants during 1972 are included. In addition, double-blind studies of lithium carbonate, as well as five other drugs not actively promoted as antidepressants in the U.S. at that time are included. Results show tricyclic antidepressants to be significantly more effective than placebo in 61 of 93 group comparisons. No study reported a placebo as more effective than a tricyclic. The two monoamine oxidase inhibitors that were actively marketed as antidepressants in the U.S. were significantly more effective than a placebo in eight of 13 comparisons. Lithium carbonate was not conclusively shown to be an effective antidepressant on the basis of eight double-blind reports. 185 references. (Author abstract)

192229 Zung, William W. K.; Gianturco, Daniel; Pfeiffer, Eric; Wang, Hsioh-Shan; Whanger, Alan; Bridge, T. Peter; Potkin, Steven G. Duke University Medical Center, Durham, NC 27705 **Pharmacology of depression in the aged: evaluation of Gerovital H3 as an antidepressant drug.** Psychosomatics. 15(3):127-131, 1974.

The therapeutic efficacy and safety of Gerovital H3 (GH3) in the treatment of depressive disorders in the aged, was evaluated by comparing it in a double-blind study with imipramine and placebo in an outpatient population. Patients were obtained from the Geriatric Psychiatric Group of the Duke University Medical Center. Tests employed included Clinical Global Impression, Depression Status Inventory, Self-rating Depression Scale, Anxiety Status Inventory, and Self-rating Anxiety Scale. The drug was found to be efficacious in the treatment of depression in the elderly and offers additional advantages in terms of its pharmacological effects and increased safety. 10 references.

192231 Smith, G. R.; Taylor, C. W.; Linkous, P. Meadowbrook Extended Care Facility, Shawsville, VA **Haloperidol versus thioridazine for the treatment of psychogeriatric patients: a double-blind clinical study.** Psychosomatics. 15(3):134-138, 1974.

Forty six geriatric patients who were behavior problems due to chronic brain syndromes or senile psychosis were treated with haloperidol or thioridazine under double-blind conditions. Both compounds were significantly effective in reducing agitation, disruptive behavior, and psychotic symptomatology. Haloperidol was effective over a broader range of symptomatology than was thioridazine. Adverse reactions were infrequent and mild. The type and incidence of side-effects was similar for both drug groups. 11 references. (Author abstract modified)

192422 Todrick, A.; Tait, A. C. Crichton Royal Hospital, Dumfries, Scotland **Laboratory assessments of antidepressive activity -- their value for clinical psychiatry and the understanding of depression.** Activitas Nervosa Superior (Praha). 16(1):58-60, 1974.

The relative potencies of imipramine, amitriptyline, chlorimipramine, desipramine, nortriptyline and protriptyline were compared to assess their value for clinical psychiatry. Clinical trials were analyzed in an attempt to work out a general rank - order of effectiveness of the compounds. If an apparent clinical superiority of imipramine over desipramine and amitriptyline over nortriptyline were to be confirmed, it would suggest that 5-hydroxytryptamine rather than noradrenaline is the amine concerned with the etiology of endogenous depression. The mood seems to be the paramount symptom and the psychomotor disturbance secondary. 15 references.

192510 Kay, Neville E.; Davies, Brian no address **A controlled trial of maprotiline (ludiomil) and amitriptyline in general practice.** Medical Journal of Australia (Sydney). 1(18):704-705, 1974.

A controlled trial of amitriptyline and a new antidepressant, maprotiline (Ludiomil) was carried out in general practice. The results show that, over the course of 4 weeks, both compounds showed similar antidepressant defects. 5 references. (Author abstract)

192521 Yaryura-Tobias, J. A.; Heller, B.; Spatz, H.; Fischer, E. North Nassau Mental Health Center, 1691 Northern Boulevard, Manhasset, Long Island, NY 11030 **Phenylalanine for endogenous depression.** Journal of Orthomolecular Psychiatry (Regina). 3(2):80-81, 1974.

Phenylalanine was administered to patients suffering from endogenous depression. Although the experimental trial was short and the dosage small, it seems that some forms of endogenous depression responded well to phenylalanine therapy, mainly with the dextrorotatory form. 7 references.

192577 Coppen, Alec; Peet, Malcolm; Montgomery, Stuart; Bailey, John; Marks, Vincent; Woods, Peter. Medical Research Council Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Thyrotrophin-releasing hormone in the treatment of depression.** Lancet (London). 2(7878):433-435, 1974.

The results of two trials of the therapeutic effects of intravenous thyrotrophin-releasing hormone (T.R.H.)in depressive patients are reported. No therapeutic action was demonstrated in a double-blind cross-over trial of T.R.H. In a further double-blind trial in which patients were given T.R.H. three times a week for 3 weeks in conjunction with a daily dose of 150mg of amitriptyline, T.R.H. again produced no therapeutic effect. There was evidence that the thyroid stimulating hormone response to T.R.H. was impaired in a proportion of the depressive patients. 12 references. (Author abstract)

192873 Asberg, Marie. Psychiatric Clinic, Karolinska Hospital, Stockholm, Sweden **Plasma nortriptyline levels -- relationship to clinical effects.** Clinical Pharmacology and Therapeutics. 16(1,Part 2):215-229, 1974.

At the Second Deer Lodge Conference on Clinical Pharmacology held in June, 1973, in Hershey, Pennsylvania, the relationship of plasma nortriptyline (NT) levels to clinical effects in patients with endogenous depression was reported. The best classification between responders and nonresponders to NT was obtained at 175ng NT per milliliter of plasma. Although the general tendency is for patients to do less well on high plasma levels, some seem to benefit from them, while others do not recover even on moderate levels. Variability in receptor sensitivity and heterogeneity within the depressive disorder may be an explanation. Monitoring NT plasma levels may be a way to increase the efficacy of treatment in patients who do not respond to standard therapy and in patients with disturbing side-effects. 107 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

187582 Burrows, Graham; Turecek, L. E.; Davies, Brian; Mowbray, Robert; Scoggins, Bruce A. Dept. of Psychiatry, University of Melbourne, Royal Melbourne Hospital, Victoria 3050, Australia **Sequential trial comparing two plasma levels of nortriptyline.** Australian and New Zealand Journal of Psychiatry (Carlton, Australia). 8(1):21-23, 1974.

In a sequential trial comparison of two plasma levels of nortriptyline, pairs of depressed patients were matched for age, sex and severity of depression and treated for 4 weeks so that plasma levels of below 49ng/ml and above 140ng/ml were obtained. Comparison of patients in regard to improvement of depression, using a sequential skew design, suggested that it is unlikely that a significant difference between the two treatment regimes would be detected. 11 references. (Author abstract modified)

188144 Hesbacher, Peter; Rickels, Karl; Clark, Edward L.; Perloff, Milton M.; Rosenfeld, Howard. no address **Are neurotic patients in psychotropic drug trials representative? A comparison of study and non-study patients in four family practices.** Social Science & Medicine (Oxford). 8(2):91-96, 1974.

Drug treated emotionally ill patients on clinical trials were compared with similar patients receiving routine drug treatment in each of four family practices to determine whether neurotic patients in psychotropic drug trials are representative. Results show an absence of selection bias in demographic characteristics. The few treatment and illness characteristics which differed between samples were attributed to the physicians' tendency to place sicker patients who have not responded well to prior drugs on controlled clinical trials. Findings indicate that the response of clincial trial patients represents a justifiable test of clinical efficacy and safety. 14 references. (Author abstract modified)

188887 Tyrer, P. J.; Lader, M. H. Dept. of Psychiatry, South Block, Southampton General Hospital, Southampton, England **Response to propranolol and diazepam in somatic and psychic anxiety.** British Medical Journal (London). No. 5909:14-16, 1974.

Six patients with chronic somatic anxiety and six patients with chronic psychic anxiety were treated with racemic propranolol (Inderal), diazepam (Valium), and placebo for 1 week each in a balanced crossover experiental design study. Clinical ratings of anxiety were made by patient and psychiatrist after each treatment. Though diazepam was generally more effective than propranolol or placebo in relieving anxiety, propranolol was more effective than placebo in patients with somatic anxiety, but not in those with psychic anxiety. It is suggested that propranolol be reserved for patients whose anxiety symptoms are mainly somatic. 25 referemces. (Author abstract modified)

189916 Razani, Javad. Psychiatric Hospital, 1934 Hospital Place, Los Angeles, CA 90033 **Treatment of phobias by systematic desensitization: comparison of standard vs methohexital-aided desensitization.** Archives of General Psychiatry. 30(3):291-293, 1974.

In a controlled (crossover) study a group of phobic neurotic psychiatric outpatients were treated with standard systematic desensitization adied by intravenously administered methohexital soidum (Brevital Sodium). Results show that desensitization is effective in reducing the severity of phobic symptoms. Methohexital aided desensitization may be significantly superior to conventional systematic desensitization in causing greater improvement of the phobic symptoms during an equal time period. The dosage range of intravenously administered methohexital sodium used in this study (up to 60mg per 50 min session) was found to be extremely safe and practical for outpatient use. 25 references. (Journal abstract)

189919 Downing, Robert W.; Rickels, Karl. 203 Piersol Building, University Hospital, 3400 Spruce Street, Philadelphia, PA 19104 **Mixed anxiety-depression: fact or myth?** Archives of General Psychiatry. 30(3):312-317, 1974.

Factors affecting the type of psychotropic medication prescribed for neurotic outpatients with a diagnosis of mixed anxiety depression are examined in a sample of 122 patients assigned to clinical trials with anxiolytics (anxiety study group) and 149 patients assigned to trials with antidepressants (depression study group). Anxiety and depression dominated the symptom profiles of all patients, but in anxiety study patients' anxiety was the more severe of the two symptoms, while in depression study patients' depression was the more severe. For physician measures, depression differed more sharply across groups; for patient measures anxiety made the greater contribution to between group differences. Multivariate analyses revealed configurational group differences involving anxiety, depression, and insomnia, and indicated that information concerning previous treatment response played an additional role in treatment assignment. 14 references. (Journal abstract modified)

191978 Fann, W. E.; Schroeder, D. H.; Mehta, N. B.; Maxwell, R. A. Department of Psychiatry, Duke University, Durham, NC **Wellbatrin in the treatment of depression.** Pharmacologist. 16(2):264, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effect of Wellbatrin, (dl-alpha-t-butylamino-3-chloropropiophenone HCl), in the treatment of depression was reported. Eleven men hospitalized for depression in the Durham VA Hospital were studied after giving informed consent. Seven of nine subjects showed improvement; those on the highest doses improved the most. Three subjects given optimum dosage improved in all parameters. Lack of improvement in two was believed due to inadequate dose and, in a third, probably due to undiagnosed schizophrenia. Wellbatrin appears to be an effective drug worthy of further evaluation in the treatment of depression. (Author abstract modified)

192066 Goldberg, Harold L.; Finnerty, Richard J.; Cole, Jonathan O. West-Ros-Park Mental Health Center, 26 Central Ave., Hyde Park, MA 02136 **Doxepin: is a single daily dose enough?** American Journal of Psychiatry. 131(9):1027-1029, 1974.

A post hoc comparison of two very similar doxepin studies that included outpatients with mixed anxiety and depression was conducted. The first study used a three times a day schedule and the second used a bedtime schedule. Findings indicate that all differences between the two treatments favor the bedtime treatment. It is suggested that these findings offer evidence for the usefulness and value of single dosage bedtime medication for anxious - depressed outpatients receiving doxepin treatment. 15 references. (Journal abstract modified)

192083 Lofft, John Gordon; Demars, Jean Pierre. 2029 Que Street, N.W., Washington, DC 20009 **A chemotherapeutic alternative to the antianxiety agents for the extended treatment of psychoneurosis.** Diseases of the Nervous System. 35(9):409-415, 1974.

The potential for abuse and dependency in antianxiety agents, notably the benzodiazepines and chlordiazepoxide, is considered, and the use of thioridazine as an alternative treatment is examined. Thioridazine, when compared on a double-blind basis to diazepam, a standard reference antianxiety agent, is shown to effectively relieve the tension and anxiety as well as other signs and symptoms associated with psychoneurosis. Thioridazine's effectiveness at low dosages coupled with its established freedom from addictive potential makes it a safe alternative for periodic substitution for the benzodiazepines or as a long-term treatment in its own right. 8 references. (Author abstract modified)

192227 Fann, William E.; Lake, C. Raymond; Majors, L. Frank. Dept. of Psychiatry, Duke University Medical Center, Durham, NC 27705 **Thioridazine in neurotic, anxious, and depressed patients.** Psychosomatics. 15(3):117-121, 1974.

Fifty nine subjects with symptoms of neurotic anxiety and depression were studied in a double-blind, placebo controlled treatment program. Thioridazine was significantly superior to placebo in alleviating symptoms of depression and anxiety in this group of anxious - depressed neurotic patients. Side-effects were mild, occurred in only a few subjects, and required none to be discontinued. Thioridazine appears to be a safe and effective agent for the treatment of persons with mild - moderate anxiety and depression. 52 references. (Author abstract)

192872 Glassman, Alexander H.; Perel, James H. Department of Biological Psychiatry, New York State Psychiatric Institute, 722 West 168th St., New York, NY **Plasma levels and tricyclic antidepressants.** Clinical Pharmacology and Therapeutics. 16(1,Part 2):198-200, 1974.

At the Second Deer Lodge Conference on Clinical Pharmacology held in June, 1973, in Hershey, Pennsylvania, the relationships between the plasma levels of tricyclic antidepressants and clinical outcome were reported from four separate studies, with a different relationship found in each of the studies. Two major underlying methodologic problems, the heterogeneity of the depressive population and individual variability in plasma protein binding, contributed to the apparent discrepancies. 15 references. (Author abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

187565 Atkinson, Michael; Hartley, David; Lunts, Lawrence H. C.; Ritchie, Alexander C. Chemistry Dept., Allen and Hanburys Research Ltd., Ware, Hertfordshire, England **Saligenin analogs of l-dopa and dl-alpha-methyl-dopa.** Journal of Medicinal Chemistry. 17(2):248-249, 1974.

The preparation of saligenin analogs of Dopa and alpha-methyl-Dopa as potential drugs for the treatment of Parkinson's disease and hypertension is discussed. The hydroxymethylation procedure for both compounds is reviewed. Studies on the utility of these analogs for hypertension or Parkinson's disease conducted in rats show little value in the treatment of either disorder. The low activity of saligenin analogs may be due to thei low substrate activity detected in vitro. 10 references.

187615 Andrews, Colin J.; Somerville, Brian. Suite 804, National Mutual Building, Darwin Place, Canberra City, Australia **Levodopa combined with MK 486 (L-alpha methyldopahydrazine) -- a peripheral decarboxylase inhibitor in Parkinson's disease.** Medical Journal of Australia (Glebe). 1(12):429-432, 1974.

A single blind trial using placebo MK 486 and active MK 486 (L-alpha methyldopahydrazine) over 20 weeks in 12 Parkinsonian patients on Levodopa (L-dopa) therapy is reported which reveals that patients on the active drug required an average of only 24.5% of their original dose of L-dopa. Clinical disability lessened and functional assessment improved slightly in 10 and eight patients respectively, who were taking the active agent. No improvement occurred in the placebo group. Combined therapy (L-dopa and MK 486) relieved nausea in all seven patients who experienced this side effect on L-dopa alone. Data indicate that MK 486 is a safe, effective peripheral decarboxylase inhibitor given in a dose of 25mg four times a day. 8 references. (Author abstract modified)

187618 Low, P. A.; Allsop, J. L.; Halmagyi, G. M. Royal Prince Alfred Hospital, Camperdown, N. S. W. 2050, Australia **Huntington's chorea: the rigid form (Westphal variant) treated with levodopa.** Medical Journal of Australia (Sydney). 1(11):393-394, 1974.

A case of the rigid form of Huntington's chorea with early onset is described, and treatment with levodopa is evaluated. In the S, a 29-year-old female, levodopa provided negligible benefit and had to be discontinued with the appearance of auditory hallucinations and ideas of reference. The patient's psychiatric status subsequently deteriorated and she was transferred to a mental hospital. The lack of involuntary move-

ments as a consequence of levodopa therapy is considered remarkable, unlike previous experience with levodopa in Huntington's chorea. 7 references. (Author abstract modified)

187866 Akiskal, Hagop S.; Beard, James D.; Fink, Robert D.; Knott, David H. Department of Psychiatry, University of Tennessee College of Medicine, 42 North Dunlap Street, Memphis, TN 38103 **Diuretic-antidepressant combination in alcoholic depressives.** Diseases of the Nervous System. 35(5):207-211, 1974.

Six patients suffering from primary affective illness and habitual excessive drinking, who had not responded to tricyclic antidepressant and/or electroconvulsive therapy, were treated with a combined diuretic - tricyclic (furosemide - amitriptyline) regimen. The patients acted as their own control. Four patients, two unipolars and two bipolars, had complete remissions, while two other patients with chronic depression showed symptomatic improvement. Implications of sodium retention for the pathogenesis of depression and alcoholism are discussed and a hypothetical positive feedback system which maintains depression and alcoholism in alcoholic depressives is proposed. 37 references. (Journal abstract)

187958 Jost, F.; Zmorski, T. Kantonale Psychiatrische Klinik, Beverin Cazis, Switzerland **/Mesoridazin (TPS 23 Sandoz) in acute psychotic states./** Mesoridazin (TPS 23 Sandoz) bei akuten psychotischen Zustanden. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 112(1):131-142, 1973.

The utility of TPS 23 Sandoz in treating various mental disorders is assessed. TPS 23 Sandoz has shown itself to be effective in agitation, tension, fear situations, alcoholism, gerontopsychiatry, and oligophrenia. The neuroleptic has also been used in acute and chronic schizophrenia and in acute psychotic states. The efficacy of TPS 23 is compared to chlorpromazine in treating psychotic disorders. The TPS 23 was more effective in calming a greater number of symptoms and there was a higher improvement rate with the TPS 23 (73% to 60%). This neuroleptic also shows minimal side-effects, even with large doses. 37 references.

187985 Carman, John S.; Shoulson, Ira; Chase, Thomas N. Neurology Unit, NIMH, Bethesda, MD 20014 **Huntington's chorea treated with lithium carbonate.** Lancet (London). No. 7861:811, 1974.

The efficacy of lithium as the sole therapeutic agent in Huntington's chorea was assessed in a double-blind crossover trial in four women and two men with moderate to advanced symptoms of the disease. Short placebo periods were instituted before and after the treatment regimen. No improvement in motor or cognitive function occurred in any of the patients. There was an apparent worsening of motor and cognitive performance during the first 4 to 7 days of lithium treatment and during a similar period immediately following lithium withdrawal. This functional deterioration was accompanied by a transient decline in serum calcium levels. It is concluded that although lithium has shown no value in treating Huntington's chorea, there is a need to examine more closely the calcium metabolism of these patients. 3 references.

188093 Gauthier, G.; Juge, O.; Birchler, A. Clinique Universitaire de Neurologie, Hopital Cantonal, CH-1211 Geneva 4, Switzerland **Parkinsonian syndromes: treatment by association of L-dopa plus decarboxylase inhibitor.** European Neurology (Basel). 11(3):133-157, 1974.

Results of treatment of 304 patients with Parkinson's disease, with L-dopa plus decarboxylase inhibitor, are presented. The efficiency of the treatment is demonstrated, and possible side-effects and difficulties of conducting such treatment are stressed. It is felt that these difficulties may be avoided by using extreme carefulness, and by a thorough followup of patients. The absence of liver toxicity of the drug used is also revealed. 16 references. (Author abstract modified)

188429 Van Woert, Melvin H.; Sethy, Vimala H.; Coleman, Mary. New Haven, CT **Treatment of action myoclonus with L-5-Hydroxytryptophan.** Neurology. 24(4):387, 1974.

The clinical and biochemical effects of L-5-Hydroxytrypophan (L-5-HTP) and other pharmacologic agents in patients with action myoclonus secondary to anoxic encephalopathy are reported. Apomorphine and low oral doses of L-dopa produced improvement in speech and myoclonic movements, whereas physostigmine salicylate and large doses of L-dopa produced aggravated symptoms. Gastrointestinal side-effects prevented further increases in the dosage of L-5-HTP. Complete relief from myoclonus and improvement of speech occurred when L-5-HTP was combined with MK 486, a peripheral L-amino acid decarboxylase inhibitor. The improvement has been maintained for a period of 6 months. The clinical improvement correlated with CSF 5-hydroxyindoleacetic acid and blood serotonin levels. It is concluded that the two combined drugs appear to be useful therapeutically for some cases of action myoclonus secondary to anoxia. Possible mechanisms of this action are hypothesized. (Journal abstract modified)

188431 Sweet, Richard D.; Bruun, Ruth D.; Shapiro, Arthur K. New York, NY **Dopamine and Gilles de la Tourette's syndrome.** Neurology 24(4):388, 1974.

The possible management of the hyperactivity associated with Gilles de la Tourette's syndrome (GTS) and dopamine (DA) treatments is discussed. A 24-year-old man gave informed consent to be tested with injections of the DA agonists apomorphine, L-dopa and ET495. Apomorphine and ET495 caused nausea and drowsiness with transient decrease in tics. The decarboxylase inhibitor MK486 and L-dopa caused hyper activity, euphoria, choreiform adventitious movements, and doubling of the activity. These ceased when medication ended. Results confirm worsening of GTS by DA increase, although agonist injections failed to show DA receptor hypersensitivity. Several possible neurological implications are also considered. (Journal abstract modified)

188446 Hoffer, A. no address **Senility and chronic malnutrition.** Journal of Orthomolecular Psychiatry (Regina). 3(1):2-19, 1974.

The hypothesis that senility is a manifestation of chronic malnutrition is considered. Evidence drawn from previous studies and the successful treatment of senility with nicotinic acid support this hypothesis. The orthomolecular approach, including use of proper nutrition plus reinforcement with megadoses of vitamins is recommended to treat and prevent senility. 56 references. (Author abstract modified)

188447 Veach, Harry O. 409 So. Plymouth Ave., Rochester, NY 14608. **Reconstructive medication.** Journal of Orthomolecular Psychiatry 3(1):20-24, 1974.

Chemotherapy for reconstructive action in a variety of intractable diseases such as multiple sclerosis, chronic alcoholism, cirrhosis of the liver, senility, and schizophrenia is

discussed. Case results are reported. The three medicines used were: azosulfamide or azulamide (A); Vitamin B Complex (Bplus); and Calcium chloride (Ca). They were used singly or in pairs but most sucessfully by combining them in one formula with administration through intravascular routes. 22 references.

188560 Fahn, Stanley. Dept. of Neurology, Columbia Univ. College of Physicians and Surgeons, 630 West 168 St., New York, NY 10032 **'On-off' phenomenon with levodopa therapy in parkinsonism: clinical and pharmacologic correlations and the effect of intramuscular pyridoxine.** Neurology. 24(5):431-441, 1974.

A treatment of parkinsonism in which levodopa was combined with carbidopa (MK-486), an inhibitor of peripheral dopa decarboxylase, was reported. Five patients with severe on - off effects of levodopa therapy were also given a combination MK-486/levodopa. Serial half hourly measurements of plasma levels of dopa, 3-O-methyldopa and homovanillic acid showed partial concordance between clinical fluctuation and plasma dopa levels in Ss receiving levodopa alone or in combination with MK-486. The combination therapy does not lessen the on - off effects except when administered in greater and more frequent doses, which were permitted by the improved gastrointestinal tolerance with MK-486/levodopa. A single intramuscular injection of pyridoxine had no clinical effect and slightly lowered subsequent plasma dopa only in the absence of carbidopa. Possible biochemical mechanisms were discussed. 35 references. (Author abstract modified)

188561 Miller, Edith Maria; Wiener, Lewis. Maimonides Medical Center, 4802 10th Ave., Brooklyn, NY 11219 **Ro 4-4602 and levodopa in the treatment of parkinsonism.** Neurology. 24(5):482-486, 1974.

The results of levodopa therapy in Parkinson's disease in combination with N-DL-seryl-N(2,3,4,-trihydroxybenzyl)-hydrazine (Ro 4-4602), a peripheral decarboxylase inhibitor, versus the results of levodopa alone were compared. With the combined treatment, the overall improvement score for extrapyramidal symptoms exceeded the optimal improvement scores achieved with levodopa alone by 25%. Gastrointestinal side-effects of levodopa were abolished in 92% of the patients and cardiovascular abnormalities in 66%. Dyskinesias were more pronounced. No toxic effects or laboratory abnormalities were noted. Levodopa dosage could be reduced by an average of 60%. The study results were compared with those obtained with another decarboxylase inhibitor, MK 468 and Ro 4-4602 was seen to be more potent. 23 references. (Author abstract modified)

188567 Safer, Daniel. School Mental Health Service, Baltimore County Dept. of Health, 505 Eastern Blvd., Essex, MD 21221 **Factors affecting outcome in a school mental health service.** Community Mental Health Journal. 10(1):24-32, 1974.

The teacher rated outcome on 70 consecutive school mental health referrals treated with brief psychiatric therapy is considered. The major clinical and outcome findings were: 40% of the children showed a hyperactive learning impaired pattern; the use of stimulant medication for the majority of the group resulted in dramatic classroom improvement; time limited therapy for academically retarded, chronically misbehaving children produced limited classroom benefits; parental antagonism toward school authorities was frequently related to student suspensions; the child's IQ was a significant positive outcome factor; and persistence in treatment was significantly greater when medication was prescribed. 24 references. (Journal abstract)

188584 Butterworth, Alfred T.; Watts, Robert D. East Louisiana State Hospital, Jackson, LA **Double-blind comparison of thiothixene, trifluoperazine, and placebo in chronic alcoholism.** Psychosomatics. 15(2):85-87, 1974.

A double-blind controlled study to evaluate the respective therapeutic potential of thiothixene, trifluoperazine and placebo in the treatment of anxious/depressive symptomatology among alcoholic patients admitted to a state hospital unit is presented. Ss were males between the ages of 21 and 56. Although results showed a relatively high placebo response, the study demonstrated the utility of thiothixene in the treatment of the group of patients. Evidence of the efficacy of thiothixene was demonstrated by all evaluation methods: Brief Psychiatric Rating Scale (BPRS); Lipman-Rickles Self Rating Scale; Zung Self Rating Scale; and the investigators' overall global impression. Trifluoperazine failed to show superiority compared to placebo in terms of overall global impression, BPRS and the Zung Self Rating Scale although it was superior to placebo in terms of the Lipman-Rickels Self Rating Scale for total score and Depression factor. No side-effects or abnormalities were observed for low dosage levels during the 3 week trial. 17 references. (Author abstract modified)

188826 Omenn, Gilbert S.; Motulsky, Arno G. no address **Pharmacogenetics and mental disease.** Psychological Medicine (London). 4(2):125-129, 1974.

In a discussion of pharmacogenetic and mental disease the striking differences among individuals in the therapeutic effectiveness and side-effects of behavior modifying drugs is stressed. The pharmacogenetics of specific drugs such as succinylcholine and nortriptyline are presented. Isoniazid, phenelzine and hydralazine are discussed in relation to their different acetylation rates in the liver. The relationship between oxidant drugs and glucose-6-phosphate dehydrogenase is outlined. The role of pharmacogenetics in the treatment of specific mental disorders such as depression schizophrenia and seizure disorders is examined. Drugs of abuse and the addiction syndromes are mentioned in addition to a consideration of the more neurological disorders such as minimal brain dysfunction and hyperkinesia. The special vulnerability of the simply inherited behavioral disorders is evaluated. 36 references.

188889 Christiansen, Claus; Rodbro, Paul; Sjo, Ole. Department of Clinical Chemistry, Glostrup Hospital, 2600 Glostrup, Denmark **'Anticonvulsant action' of vitamin D in epileptic patients? A controlled pilot study.** British Medical Journal (London). No. 5913:258-259, 1974.

The frequency of epileptic seizures was observed in a controlled therapeutic trial on 23 epileptic inpatients before and after treatment with vitamin D, or placebo, in addition to anticonvulsant drugs. The number of seizures was reduced during treatment with vitamin D but not with placebo. The effect was unrelated to changes in serum calcium or magnesium. Results indicate that epileptics should be treated prophylactically with vitamin D. 5 references. (Author abstract)

189174 Lerman, Pinchas; Kivity-Ephraim, Sarah. Neuropediatric Clinic, Beilinson Medical Center, Tel Aviv University Medical School, Petah Tikva, Israel **Carbamazepine sole anticonvulsant for focal epilepsy of childhood.** Epilepsia (Amsterdam). 15(2):229-234, 1974.

Carbamazepine (Tegretol) was used as sole anticonvulsant in 18 boys and 22 girls with benign focal epilepsy with Rolandic spikes. In 12 patients, carbamazepine was the first and only drug used, whereas in the others various drugs and drug com-

binations had previously been administered. The following conclusions were drawn: carbamazepine is a highly effective drug in focal epilepsy of childhood, as effective as barbiturates and diphenylhydantoin, less toxic, and more convenient to use. Carbamazepine improved the behavior, ability to concentrate, and performance in school of 80% of the children. At effective dose levels, there were remarkably few side-effects. 13 references. (Author abstract)

189403 Fann, W. E.; Lake, C. R.; Gerber, C. J.; McKenzie, G. M. Department of Psychiatry, Baylor College of Medicine, 1200 Moursund Avenue, Houston, TX 77025 **Cholinergic suppression of tardive dyskinesia.** Psychopharmacologia (Berlin). 37(2):101-107, 1974.

The cholinergic suppression of tardive dyskinesia (TD) was studied. It is suggested that TD, a hyperkinetic disorder associated with long-term neuroleptic treatment, may be a manifestation of imbalance of opposing dopamine (DA) and acetylcholine (ACh) dependent systems in the central nervous system (CNS). Dopamine blocking agents gave some transient relief of symptoms. Physostigmine, an anticholinesterase which enhances CNS acetylcholine action, was given to seven subjects with TD and measurements of their pathological movements were made 45 min before and 24 hr after administration. All seven subjects showed significant suppression of movement at 24 hr. Many showed measurable decrement at 45 min. Side-effects were minimal and transient. It is concluded that physostigmine suppresses movements of TD. 15 references. (Author abstract)

189502 Bauer, Raymond B.; McHenry, John T. Department of Neurology, Wayne State University, 3990 John R Street, Detroit, MI 48201 **Comparison of amantadine, placebo, and levodopa in Parkinson's disease.** Neurology. 24(8):715-720, 1974.

A double-blind crossover trial of amantadine hydrochloride and placebo, each given for 3 week periods, was performed on 40 outpatients with Parkinson's disease. Conventional antiparkinsonian drugs were continued during the 6 week period. Amantadine was effective by objective measurements (timed tests) and subjective ratings of tremor and rigidity. Amantadine produced an average 16% objective improvement over baseline in the 40 patients. At the end of a third 3 week period, during which conventional drugs had been stopped, amantadine produced a 21% improvement compared with baseline. After 6-9 weeks of levodopa added to amantadine, there was a 28% improvement over baseline. It is concluded that amantadine appears to be a useful adjunct in the treatment of Parkinson's disease, and amantadine and levodapa together may be effective combination therapy. 10 references. (Author abstract)

189778 Meadow, Roy. Department of Pediatrics and Child Health, University of Leeds, 27 Blundell Street, Leeds LS1 3ET, England **Drugs for bed-wetting.** Archives of Disease in Childhood (London). 49(4):257-258, 1974.

The value of drugs in the management of nocturnal enuresis is examined, and the variety of drugs tried is reviewed, including imipramine and amitriptyline. It is shown that complete cessation of wetting is less common than a mere reduction in the number of wet nights, with a high proportion of relapse. It is suggested that their most effective use is in children who need quick proof that it is possible to be dry or who need to be dry quickly for a specific occasion, such as school camp. 6 references.

189926 Rosenberg, Chaim M. Harvard Medical School, Boston City Hospital, Boston, MA 02118 **Drug maintenance in the outpatient treatment of chronic alcoholism.** Archives of General Psychiatry. 30(3):373-377, 1974.

In a study of drug maintenance in the outpatient treatment of chronic alcoholism, 123 alcoholics attended counseling sessions twice weekly and were assigned to one of four groups to receive, under supervision, disulfiram, chlordiazepoxide, a multivitamin preparation, or no medication. Those patients ingesting drugs at the clinic were also given a small quantity to take at home between clinic visits. During the first 20 week followup period, the chlordiazepoxide group had the highest rate of retention followed by the disulfiram, vitamin, and the no medication groups. After that period, differences between the groups were lost. Patients who were referred for treatment by the courts following a conviction for drunken driving attended substantially longer than the volunatry patients, regardless of the treatment condition to which they were assigned. 15 references. (Journal abstract modified)

190061 Tennent, Gavin; Bancroft, John; Cass, James. Special Hospitals Research Unit, Broadmoor Hospital, Crowthorne, Berks., England **The control of deviant sexual behavior by drugs: a double-blind controlled study of benperidol, chlorpromazine, and placebo.** Archives of Sexual Behavior. 3(3):261-271, 1974.

A method for assessing the effect of drugs on sexual drive and arousability is reported to compare the effect of a butyrophenone, benperidol, with chlorpromazine and placebo. Measures of change used included sexual behavior ratings, self-ratings, and penile erections to erotic fantasy, slides, and film. The study involved 12 pedophiliac sexual offenders. Results showed no significant difference between benperidol and the other two drug conditions, except in the self-rating of frequency of sexual thoughts, which was lower on benperidol. The libido reducing effects of benperidol are presumed to be weak and unlikely to be sufficient to control serious antisocial sexual behavior. The research method is suitable for assessing the effects of other drugs or hormones on sexual behavior. 27 references. (Author abstract modified)

190095 Matsumoto, Keizo; Ohmoto, Takashi; Beck, Hiroichi. Dept. of Neurological Surgery, Okayama Univ. School of Medicine, Okayama, Japan **Clinical evaluation of amantadine therapy for Parkinsonism and the side effects -- in cases of thalamic surgery and L-dopa therapy.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 28(1):1-10, 1974.

Amantadine therapy combined with stereotaxic thalamic surgery and/or L-dopa therapy is evaluated in a consecutive series of 21 cases of primary Parkinsonism or the so called idiopathic Parkinsonism with insidious onset, after middle age, of the typical manifestation of increasing rigidity, tremor and bradykinesia. Side-effects associated with this combined therapy were investigated also. Findings indicate that administration of amantadine ameliorated rigidity and bradykinesia rather than tremor in patients with Parkinsonism. When prescribed in combination with L-dopa, amantadine enhanced the therapeutic effects of the latter. Amantadine efficacy did not differ significantly between patients who underwent thalamotomy and that of unoperated cases. Side-effects associable with administration of amantadine were noted in 43% of cases. Dosages recommended to obtain maximal therapeutic effect with least side-effects are noted. 19 references.

190138 Erenberg, Gerald. Center for Child Development, Morrisania City Hospital, Bronx, NY **Psychotropic drugs --**

harm or help. Journal of the National Medical Association. 66(3):214-216, 218, 1974.

The use of psychotropic drugs, especially of the stimulant drugs dextroamphetamine (Dexedrine) and methylphenidate (Ritalin) for 'problem' children of school age, is discussed. Reasons for and against the use of the drugs for this particular purpose are reviewed; alternatives to drugs are mentioned and reasons for the effective use of the drugs are outlined. 16 references.

190194 Kochar, Mahendra S.; Itskovitz, Harold D.; Sasse, Edward A.; Baker, John D.; Doumas, Basil T. 2388 North Lake Drive, Milwaukee, WI 53211 **Dose-related alterations in metabolism of levodopa: possible mechanism for hypotensive effect.** Journal of Clinical Pharmacology. 14(8&9):448-454, 1974.

The metabolism of levodopa was studied in 23 patients with Parkinsonism treated with this drug by determining the urinary excretion of metabolic products of levodopa. The absolute quantity of urinary dopamine and its metabolites varied directly with the dose of the drug. No increases occurred in the excretion of norepinephrine plus epinephrine (NE+E) and their metabolites. The ratio of 3,4-dihydroxy-phenylacetic acid (DOPAC) plus 3-methoxyl-4-hydroxyphenylacetic acid (HVA) to dopamine did not change significantly with different doses of levodopa. A negative correlation existed between the ratio of 3-methoxy-4-hydroxymandelic acid to NE+E and metanephrines. Blood pressure levels were significantly lower in patients who received larger doses of levodopa. 11 references.

190336 Tansella, Michele; Zimmerman-Tansella, Christa; Lader, Malcolm. Cattedra di Psicologia, Instituto di Clinica, Psychiatrica di Verona, Italy **The residual effects of N-desmethyldiazepam in patients.** Psychopharmacologia (Berlin). 38(1):81-90, 1974.

In an examination of residual drug effects, 60 anxious inpatients complaining of insomnia were treated with either 20mg of N-desmethyldiazepam, 10mg of this drug, 200mg of amylobarbitone sodium, or placebo, given at night. The hypnotic effects of these treatments were assessed by self-rating, psychiatrists' ratings and night nurses' observations after one night's treatment and after a week of treatment and compared with pretreatment values. The residual effects of the treatments were estimated 12 h after ingestion using a series of cognitive and motor tasks. No significant differences between the treatments were found after one night. After the week of treatment, the benzodiazepine groups were achieving the best quality of self-rated sleep with fewest subjective feelings of hangover. Some improvement in performance was found over time for all groups. On two motor tests, the higher dose of N-desmethyldiazepam was associated with less improvement, i.e.,some impairment relative to placebo was detected. 15 references. (Author abstract)

190380 Fann, William E.; Lake, C. Raymond. Department of Psychiatry, Baylor College of Medicine, 1200 Moursund Avenue, Houston, TX 77025 **On the coexistence of Parkinsonism and tardive dyskinesia.** Diseases of the Nervous System. 35(7):324-326, 1974.

The coexistence of parkinsonism and tardive dyskinesia (TD) was examined in three male subjects. These two neurological conditions can coexist in the same subject and the present treatment methods for one may accentuate the other; agents which work to meliorate TD intensify symptoms of parkinsonism, just as those which work to meliorate parkinsonism intensify TD. It is recommended that physicians use caution in prescribing neuroleptic agents, use the lowest possible dose for long-term therapy and make frequent reassessment of the patient's condition. 8 references.

190670 Petrozzi M., Carlos; Del Carpio W., Jaime Departmento de Medicina, Universidad Peruana Cayetano Heredia **/The stiff-man syndrome./** El sindrome del hombre tieso. Revista de Neuro-Psiquiatria (Lima). 36(1):34-45, 1973.

The case history of a 55-year-old unmarried woman, a mestiza, suffering from the first known Peruvian case of stiff-man syndrome is reported. The case is of interest because the disorder is unknown to the majority of those who should be aware of the syndrome, and while rare, ignorance of it is unjustified. Moreover, the patient can be helped by therapeutic agents. The symptoms in this case were convulsions and falling to the ground without losing consciousness. A history of lumbar pain and sensations of spasms in the lower limbs dated back 20 years. Pathological history, family history, results of physical and neurological examinations, and of other tests, are detailed. The pathogenic mechanisms of the syndrome are emphasized, as are the simplicity and effectiveness of treatment with diazepam. 23 references.

191140 Singh, A. N. Dept. of Psychiatry, McMaster University, Hamilton, Ont., Canada **Use of chemotherapy as anti-suicidal prophylaxis.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):32-36, 1974.

The developing states of suicidal impulse are discussed and the importance of utilizing the various groups of drugs in the most responding stages of suicide is discussed in terms of the results of a study of 57 patients with the diagnosis of depression with suicidal risk. It is noted that depressive states make up about half the mentally ill patients who show suicidal impulse. 8 references. (Author abstract modified)

191192 Keegan, David L.; Pettigrew, Andrew; Parker, Zilla. Dept. of Psychiatry, Univ. of Saskatchewan, Univ. Hospital, Saskatooon, Saskatchewan, Canada **Amitriptyline in the psychotic states of Down's Syndrome: the comparison of two cases.** Diseases of the Nervous System. 35(8):381-383, 1974.

Two cases of psychoses occuring in Down's Syndrome, which were managed by the use of Amitriptyline, a tricylic antidepressant, are discussed. The cases differed significantly in presentation, primarily in terms of the amount of motor activity and behavioral symptoms. Explanations as to similarities in these cases and in other psychotic disorders in Mongoloids are presented. It is felt that serotonin metabolism should be further studied in these cases. 14 references. (Author abstract modified)

191533 Fann, William E.; Lake, C. R.; McKenzie, G. M. Department of Psychiatry, Duke University Medical Center, Durham, NC **Adrenergic and cholinergic factors in extrapyramidal disorders.** Psychopharmacology Bulletin. 10(3):52-53, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a study was reported in which groups of Ss manifesting various extrapyramidal disorders were given the cholinergic substance physostigmine, and the adrenergic - dopaminergic substances methylphenidate and amantadine to determine their roles in the disturbances. Disorders included idiopathic and drug induced parkinsonism, Huntington's disease (HD), rigid Huntington's disease, tardive dyskinesia (TD), acute drug induced dyskinesia, and acute drug induced

dystonia. The finding that methylphenidate increased symptoms was consistent with current theories of TD, while suppression of movements in TD and HD through increased CNS acetylcholine activity suggested reduced acetylcholine function. The reversal of acute neuroleptic induced dystonic conditions and parkinsonism by anticholinergic amantadine, and methylphenidate suggested that reduced dopamine activity is present. The fact that acute dyskinesias responded inconsistently to methylphenidate and may be aggravated by enhancing cholinergic activity suggests that not all of these conditions are simply due to reduction in dopamine activity but are due to effects on acetylcholine as well. Overall data suggest involvement of both acetylcholine and dopamine dependent systems and have clinical implications.

191614 Selby, George. Royal North Shore Hospital, Sydney, Australia **Long-term treatment with laevodopa.** Neurology India (Bombay). 20(Supplement II):215-219, 1972.

Fifty one Parkinsonism patients (idiopathic paralysis agitans) were observed before and after long-term treatment with levodopa to determine if treatment with levodopa can prevent the natural progression of the disease and if the earlier therapeutic success is maintained, lost, or enhanced. The effect of treatment was not immediate and there was a direct relationship between therapeutic success and duration of therapy. It is hypothesized that some disuse atrophy of the cell body or axon of the neuron, or more probably of the synaptic vesicles which contain the transmitter substance, may occur. It is conceivable that the dopamine derived from therapeutic administration of levodopa could result in a general proliferation of such vesicles. 4 references.

192005 Cooper, S. D.; Sellers, E. M.; Khouw, V.; Zilm, D. H.; Israel, Y. Addiction Research Foundation, University of Toronto, Toronto, Canada **Lithium treatment during ethanol ingestion and withdrawal.** Pharmacologist. 16(2):304, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, lithium (Li) treatment during alcohol ingestion and withdrawal was studied in 18 hospitalized chronic alcoholics in a randomized double-blind study. There was no effect of Li on systolic pressure, heartrate, hand tremor amplitude, sleep electroencephalogram, urinary norepinephrine, epinephrine, total metanephrine, or vanilmandelic acid in either the alcohol or withdrawal phase. Li decreased the total number of withdrawal symptoms in II and III. Li did not affect the Addiction Research Center Inventory scores on the Alcohol or Drug Estimation (DE) Scales on days 1 to 3. Scores on the DE scale were closer to normal on days 4 to 9 in II. Performance on a motor tracking tasks was restored to normal in Li treated groups. No adverse effects of Li treatment occurred. Li effectively decreases some signs and symptoms of mild alcohol intoxication and withdrawal. (Author abstract modified)

192068 Favazza, Armando R.; Martin, Patricia. Department of Psychiatry, School of Medicine, University of Missouri, Columbia, MO 65201 **Chemotherapy of delirium tremens: a survey of physicians' preferences.** American Journal of Psychiatry. 131(9):1031-1033, 1974.

A survey of physicians' preferences in the chemotherapy of delirium tremens is discussed. Findings indicate that out of 101 useful responses to a questionnaire sent to selected experienced physicians, 86 choose benzodiazepines as a primary drug of choice. Of these, 64 favor chlordiazepoxide and 22 favor diazepam. Results indicate that the overall mortality of the patients treated is low. 5 references. (Journal abstract modified)

192419 Roth, B.; Faber, J.; Nevsimalova, S.; Tosovsky, J. Department of Neurology, Charles University Medical Faculty, Prague, Czechoslovakia **The influence of imipramine, dexphenmetrazine and amphetamine-sulphate on the composition of diurnal sleep of narcoleptics.** Activitas Nervosa Superior (Praha). 16(1):52-53, 1974.

The influence of imipramine, dexphenmetrazine and amphetamine sulfate in the treatment of narcolepsy was studied in 13 adult narcoleptics. Imipramine is very effective against cataplexy, sleep paralysis and hypnagogic hallucinations, while desphenmetrazine and amphetamine have much weaker and less constant effects. All three drugs lead primarily to changes in the ratio of NREM sleep versus REM sleep duration without influencing significantly the total sleep time. 7 references.

192527 Liden, Sture; Gottfries, Carl-Gerhard. Department of Dermatology, University Hospital, S-90185 Umea, Sweden **Beta-blocking agents in the treatment of catecholamine-induced symptoms in musicians.** Lancet (London). 2(7879):529, 1974.

A double-blind crossover experiment using volunteers from a professional orchestra investigated the use of a beta blocking agent (alprenolol chloride, 'Aptin') for the treatment of catecholamine induced symptoms. The absolute severity of the symptoms after treatment fell for active substance and placebo, for both symptoms of the catecholamine syndrome and symptoms not directly catecholamine related. Comparisons on relative values, preference, and global assessment show the active substance to be more effective. 1 reference.

192589 Kelly, Michael G. Jervis St. Hospital, Dublin 1, Ireland **Trial of sustained release amitriptyline on enuresis.** Journal of the Irish Medical Association (Dublin). 67(12):343-344, 1974.

A double-blind crossover study was designed to evaluate a sustained release form of amitriptyline in the treatment of nocturnal enuresis in mentally handicapped patients. Data based on comparison of amitriptyline and a placebo in 22 patients indicates that sustained release amitriptyline may be of value in treating nocturnal enuresis in mild to moderately handicapped male patients. 5 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

188121 Snyder, Solomon H.; Unger, Sanford; Blatchley, Robert; Barfknecht, Charles F. Dept. of Pharmacology, Johns Hopkins School of Medicine, 725 N. Wolfe St., Baltimore, MD 21205 **Stereospecific actions of DOET (2,5-dimethoxy-4-ethylamphetamine) in man.** Archives of General Psychiatry. 31(1):103-106, 1974.

A comparison of the psychotropic effects of isomers of DOET (2,5-dimethoxy-4-ethylamphetamine) a 'psychedelic' methoxyamphetamine, in normal human subjects is reported. The (-) 'R' isomer is about four times as potent as the (+) 'S' isomer, thus specifying the psychoactive conformation of the drug. This clinical study represents a novel approach to determining the molecular conformation of a drug at its receptor site. 22 references. (Author abstract modified)

188229 Winter, J. C. Dept. of Pharmacology and Therapeutics, School of Medicine, State University of New York, Buffalo, NY 14214 **Hallucinogens as discriminative stimuli.** Federation Proceedings. 33(7):1825-1832, 1974.

A preliminary attempt to test the hypothesis that those pharmacologic properties which serve to distinguish hallucinogens and nonhallucinogens in man are reflected in distinctive stimuli

in infrahuman species is reported. Operant behavior which is reinforced only in the presence of a specified stimulus soon occurs with greater frequency in the presence of the stimulus than in its absence and the behavior is then said to be under the control of the stimulus. In addition to well known sensory stimuli, it has been known for some time that a drug may serve as a discriminative stimulus. A general method is presented for the comparison of the stimulus properties of pharmacologic agents and the method is illustrated by a study of mescaline, its structural isomer, 2,3,4-trimethoxyphenylethylamine, and 3,4-dimethoxyphenylethylamine (DMPEA). 53 references. (Author abstract modified)

189101 Schultes, Richard Evans; Hofmann, Albert. no address **The botany and chemistry of hallucinogens.** Springfield, Ill., Charles C Thomas, 1973. 251 p. $14.95.

All known and reported hallucinogenic plants are surveyed. Introductory chapters deal with the historical development of the field, its definition, and the general botanical and chemical relationships thus far known. Each species of hallucinogenic plant is carefully described, together with its distribution, use, chemistry, and, in some instances, reference to synthesis of active agents. A chapter on plants of possible or suspected hallucinogenic use is included. Many illustrations and references are included.

189744 Panton, Yvonne; Fischer, Roland. Maryland Psychiatric Research Center, Box 3235, Baltimore, MD 21228 **Hallucinogenic drug-induced behavior under sensory attenuation: prediction of response to psilocybin.** Archives of General Psychiatry. 28(3):434-438, 1973.

To examine hallucinogenic drug induced behavior, eight 'stable' and four 'variable' college age subjects were given 160mg/kg psilocybin under conditions of sensory attenuation. Stability was defined by the magnitude of the standard deviation (SD) on handwriting area under predrug conditions. Only the variable subjects, the large standard deviants, responded to the drug with a significant decrease in mean pulse rate and increase in handwriting area. They also reported consistently more intense experiences under psilocybin than the small standard deviants. It is concluded that the degree of variability on perceptual - behavioral measures, such as the SD on handwriting areas, is significantly related to, and therefore a predictor of, the intensity of the ensuing drug induced experience. 23 references. (Author abstract modified)

189754 Sierra, M. Rojo; Ubago, J. Giner; Romero, R. Jimenez. Departamento de Psiquiatria de la Universidad de Valencia, Spain /**Mythicizing elements in experimental psycholysis.**/ Los mitologemas en la psicolisis experimental. Revista de Psiquiatria y Psicologia Med. de Europa y America Lat. (Madrid). 11(3):145-161, 1973.

The evolution of the myths of primitive man, types of myths, and the need of primitive man for myths to explain what he could not comprehend, are reviewed. Causes of mythicizing in patients treated with LSD are investigated. The results of studying 31 patients of both sexes, 25 to 45 years of age, who had mythical experiences are tabulated. The similarity of myths experienced by paraphrenetic patients and patients treated with LSD is noted, and myths that occur under LSD treatment but not in paraphrenetic patients are listed. The delirious ideas attributed to paranoid schizophrenics and paraphrenetics are discussed; the content of these ideas is shown to be very similar to the myths of ancient peoples. Mentally deranged patients apparently mythicize in a manner similar to that indulged in by ancient man when confronted by mysterious forces. 5 references.

191535 Mandel, Lewis R. Department of Biochemistry, Merck Institute for Therapeutic Research, Rahway, NJ **Dimethyltryptamine: its biosynthesis and possible role in mental disease.** Psychopharmacology Bulletin. 10(3):55-56, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the biosynthesis of N,N-dimethyltryptamine (DMT), a hallucinogenic agent, was discussed, as well as its possible role in schizophrenia. DMT has been reported to be present in elevated levels of some schizophrenic patients and so was implicated in this disease. Further study revealed that DMT fulfills other criteria required for its consideration in this condition: in single doses, it produces some schizophrenic symptoms; DMT precursors and enzymes for its synthesis are presented in man; in several species, tolerance does not develop with repeated administration; and the extremely short life of DMT in vivo suggests it may be too rapidly metabolized to use blood and urine concentrations to differentiate schizophrenics from normals. 7 references.

192874 McLaughlin, J. L. School of Pharmacy and Pharmacal Sciences, Purdue Univ., Lafayette, IN 47907 **Peyote: an introduction.** Lloydia. 36(1):1-8, 1973.

An introduction to literary information on the peyote cactus is presented. The use of peyote by the Indians of north central Mexico and the southwestern U.S.,as a medicine, an amulet and a hallucinogenic religious sacrament, is described. A plant description and the scientific and common names of the plant are included. The abuse of peyote and mescaline is less than might be expected, due the bitter taste and nausea caused by peyote and the low potency of mescaline as a hallucinogen. The need for further research and for a symposium on the chemical progress of research is suggested. 73 references.

192875 Kapadia, Govind J.; Fayez, M. B. E. Dept. of Pharmacognosy and Natural Products, College of Pharmacy, Howard Univ., Washington, DC 20001 **The chemistry of peyote alkaloids.** Lloydia 36(1):9-35, 1973.

The chemistry of peyote alkaloids is reported, and early chemical studies are reviewed. The synthetic approaches to the following constituents of peyote are described: the phenethylamines; the tetrahydroisoquinilines; the conjugates with Krebs cycle acids; and the pyrrole derivatives. The mass spectra of the peyote constitutents is also discussed. A tabular listing of peyote constituents includes the name, formula, the melting point, the boiling point and the substituents of each constituent. 194 references.

192876 Paul, A. G. College of Pharmacy, Univ. of Michigan, Ann Arbor, MI 48104 **Biosynthesis of the peyote alkaloids.** Lloydia. 36(1):36-45, 1973.

The biosynthesis of the peyote alkaloids is reviewed. The in vivo biosynthesis of the phenethylamine moiety is described. The enzymatic processes involved in the biosynthesis of the peyote alkaloids are presumed to be hydroxylation, O-methylation and cyclization. The purification procedure and certain of the properties of the partially purified enzyme are listed. The origins of the C-1 and C-1, C-9 units of the tetrahydroisoquinoline alkaloids are discussed. 21 references.

192877 Shulgin, Alexander T. 1483 Shulgin Rd., Lafayette, CA **Mescaline: the chemistry and pharmacology of its analogs.** Lloydia. 36(1):46-58, 1973.

The chemistry and pharmacology of the analogs of mescaline are presented. The substituted phen-

ylisopropylamines carry the carbon skeleton of amphetamine, as found in natural bases such as ephedrine. Ring substitution arrangements that imitate the peyote alkaloids and the phenylpropenes from the essential oils, have led to a number of hallucinogens generally more potent than mescaline. They all reflect some botanical precedent. Other analogs are based largely on changes in the length of the carbon chain or in the nature of the substituent in the four position. The shortening of the chain decreases the observed potency, but any lengthening changes the pharmacological action from hallucinogenesis to relaxants or to psychic energizers. The para-substitution changes involving alkyl groups, halides or cyclic ethers have led to a retention of mescaline like activity, but with a consistent increase in potency. 52 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

187350 Ashton, Heather; Millman, J. E.; Telford, Rosemary; Thompson, J. W. Dept. of Pharmacology, University of Newcastle upon Tyne, Newcastle, England **The effect of caffeine, nitrazepam and cigarette smoking on the contingent negative variation in man.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 37(1):59-71, 1974.

The effects of caffeine, nitrazepam and cigarette smoking on the contingent negative variation (CNV) of man were studied. Caffeine increased the magnitude of the CNV, nitrazepam decreased it and smoking was followed by changes in both directions. Correlations of the percentage change in CNV magnitude with rate of nicotine intake and degree of extraversion suggested that the rate of nicotine intake in extraverted smokers was slower and associated with stimulant effect, while in introverted smokers the rate was faster and associated with a depressant effect in terms of changes in CNV magnitude. 48 references. (Author abstract modified)

187398 Post, Robert M.; Goodwin, Frederick K. Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Studies of cerebrospinal fluid amine metabolites in depressed patients: conceptual problems and theoretical implications. (Unpublished paper).** Bethesda, MD, NIMH, 1974. 13 p.

Potential neurotransmitters and their metabolites in cerebrospinal fluid were studied in various depressive states. Results indicate that alterations in amine systems that are manifest after 3 weeks of phenothiazine treatment may better correlate with the time course of onset of maximal clinical antipsychotic or antidepressant effects than acute biochemical changes. The regulatory and long-term compensatory mechanisms within and between neurotransmitter systems may be crucially related to the pathophysiology of abnormal behavior and its therapies. Instead of a model suggesting a single biochemical abnormality in mania or depression, findings indicate the importance of multiple alterations, subtle but critical changes in neurotransmitter ratios and sensitivities and multiple feedback adjustments to psychoactive stimuli and drugs. 70 references.

187812 Clark, S. C.; Greene, C.; Karr, G. W.; MacCannell, K. L.; Milstein, S. L. Division of Pharmacology and Therapeutics, School of Medicine, Univ. of Calgary, Calgary, Alberta T2N 1N4 **Cardiovascular effects of marihuana in man.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(3):706-719, 1974.

The cardiovascular effects of marihuana in man was studied in 28 subjects, matched by sex and Cannabis experience, who received by controlled inhalation, under single-blind and double-blind conditions, 600mg marihuana placebo and marihuana. Forearm, venous and arterial pressures, forearm blood flow, and heartrate were recorded while supine. Derived functions such as 'dp/dt', regional arterial resistance, and venous compliance were calculated from these variables. Placebo produced no intoxication or consistent physiological response, but marihuana produced intoxication in all Cannabis experienced and half of the nonexperienced subjects. Cardiovascular responses occurred in response to marihuana in the absence of intoxication, indicating that they were not psychogenically mediated. Inhibition of vagal tone may contribute to the tachycardia seen with marihuana, and reflexly mediated sympathetic responses may be muted in the presence of marihuana. 21 references. (Author abstract modified)

187877 Mars, Harold. Division of Medicine, Department of Neurology, Mt. Sinai Hospital, Case Western Reserve University, Cleveland, OH 44106 **Levodopa, carbidopa, and pyridoxine in Parkinson disease.** Archives of Neurology. 30(6):444-447, 1974.

The metabolic interactions of levodopa, pyridoxine, and carbidopa, a peripheral decarboxylase inhibitor, were studied in 15 long-term, levodopa treated Parkinson disease patients. Pyridoxine reduced plasma dopa levels 67% but enhanced homovanillic acid synthesis 49%. Carbidopa potentiated plasma dopa, inhibited homovanillic acid synthesis, and minimized the effects of pyridoxine. The decarboxylase activity index following pyridoxine administration increased 483% and 136% for plasma and urine respectively. Carbidopa effected a 77% and 94% reduction. It is suggested that pyridoxine accelerates systemic metabolism of levodopa, decreasing availability of the amino acid to brain parenchyma. The combination of levodopa and carbidopa prevents the loss of levodopa effect produced by exogenous pyridoxine. 18 references. (Journal abstract)

187933 Perel, James M.; Levitt, Morton; Dunner, David L. New York State Psychiatric Institute, 722 West 168 Street, New York, NY 10032 **Plasma and cerebrospinal fluid probenecid concentrations as related to accumulation of acidic biogenic amine metabolites in man.** Psychopharmacologia (Berlin). 35(1):83-90, 1974.

The oral administration of probenecid to depressed patients results in marked increases in the acidic metabolites of biogenic amines in the cerebrospinal fluid (CSF), and higher plasma and CSF probenecid concentrations were found in this study. The binding of probenecid to plasma proteins for each patient was determined to examine the pharmacodynamics of probenecid distribution. The ratio of probenecid in CSF to the calculated free probenecid in plasma was higher and more constant than previously noted. At the higher dose levels, probenecid successfully competes with the active transport process for biogenic amine acidic metabolites and also appears to block its own removal from CSF. 27 references. (Author abstract modified)

188119 Perez-Reyes, Mario; Timmons, Martha C.; Wall, Monroe E. University of North Carolina School of Medicine, Chapel Hill, NC 27514 **Long-term use of marihuana and the development of tolerance or sensitivity to delta9-tetrahydrocannabinol.** Archives of General Psychiatry. 31(1):89-91, 1974.

The development of tolerance or sensitivity to delta9-tetrahydrocannabinol (delta9-THC) over long-term use was investigated in human Ss. A group of 15 subjects who have used marihuana infrequently and a group of 15 subjects who have

used the drug frequently were intravenously infused with delta9-tetrahydrocannabinol. In spite of the marked differences in marihuana use, the groups did not differ significantly in the amount of delta9-THC necessary for its effects to be perceived, to accelerate the heart 25% above the baseline levels, the total dose administered, the maximum level of 'high,' the maximum heartrate acceleration, and the heartrate acceleration observed 15 minutes after the beginning of the infusion. This is evidence that marihuana, as currently used by young Americans does not produce tolerance or sensitivity to its effects. 6 references. (Author abstract)

188120 Renault, Pierre F.; Schuster, Charles R.; Freedman, Daniel X.; Sikic, Branimar; de Mello, Dorothy Nebel; Halaris, Angelos. Dept. of Psychiatry, University of Chicago, 950 E. 59th St., Chicago, IL 60637 **Repeat administration of marihuana smoke to humans.** Archives of General Psychiatry. 31(1):95-102, 1974.

Tolerance to marihuana (THC) was investigated in two experiments. Four men were given smoke from 435mg of marihuana twice a day for 10 days preceded and followed by 3 days of a placebo twice a day; three additional men were given a higher dose (2.8% THC). Time estimation was disrupted on the higher dose and gradually improved. Heartrate increase did not show tolerance. Enhancement of postural cardiovascular responses, when present, decreased in duration in three subjects. One developed a brief toxic psychosis, another pneumonitis of uncertain etiology. Dysphoric and psychotoxic effects were evident as a cumulative effect of the high dose. Three additional men were given the low dosage once a week for 6 to 8 weeks, and time estimation and heartrate changes were similar to those seen with frequent administration at that dose. Tolerance, recently reported in man, probably requires more frequent administration or a different dosage than the schedules employed here. 22 references. (Author abstract)

188350 Chiodini, P. G.; Liuzzi, A.; Botalla, L.; Cremascoli, G.; Silvestrini, F. Center of Endocrinology, Ospedale Maggiore di Milano, Milan, Italy **Inhibitory effect of dopaminergic stimulation on GH release in acromegaly.** Journal of Clinical Endocrinology and Metabolism. 38(2):200-206, 1974.

The inhibitory effect of dopamine on gonadotropic hormone (GH) secretion was examined in acromegalic patients. In 15 out of 19 acromegalic patients, oral administration of L-dopa (500mg) determined a conspicuous fall in GH plasma levels. In 8 out of these 15 patients the inhibitory effect was constantly observed when the test was repeated; apomorphine administration (0.75mg sc) was also followed by a significant fall of plasma levels of GH. These results are consistent with the hypothesis that the inhibitory effect of L-dopa is mediated by an activation of dopaminergic receptors at the hypothalamic or at the pituitary level. Chronic administration of L-dopa does not achieve any stable reduction of plasma GH levels because of the shortness of the inhibitory effect. L-dopa, associated with an inhibitor of decarboxylase, does not give better results. 19 references. (Author abstract)

188421 Sweet, Richard D.; McDowell, Fletcher H. New York, NY **Plasma dopa and functional oscillations after chronic treatment of Parkinson's disease.** Neurology. 24(4):358-359, 1974.

Fluctuations in motor ability in Parkinsonian patients who have been treated by L-dopa for a long period were studied. Plasma dopa and CSF HVA and 5HIAA during 'on' (mobile with dyskinesia and imbalance) and 'off' (akinetic or tremulous) episodes were measured in twelve patients. Plasma dopa was significantly higher during 'on' spells than during the akinetic spells. However, plasma dopa levels were not high during each on or low during each off episode. Nine patients were given a low protein diet in an attempt to equalize dopa absorption from the gut throughout the day. Two patients improved remarkedly. Plasma dopa levels were significantly higher during low protein intake than during regular diet. CSF samples showed no significant differences. It is concluded that peripheral handling of levadopa is important in the 'on-off response.'(Journal abstract modified)

188428 Martin, Jospeh B.; Lal, Samartha; Tolis, George; Friesen, Henry G. Montreal, Quebec, Canada **Role of dopaminergic mechanisms in regulation of growth hormone and prolactin secretion in man.** Neurology. 24(4):387, 1974.

The effects of L-dopa and apomorphine (APO) were compared in normal subjects and in patients with elevated serum growth hormone (hgH) or prolactin (hPRL) levels. Dopaminergic mechanisms and the hypothalamic regulation of growth hormone and prolactin secretion were studied. APO doses caused elevation of serum hGH levels in each of the nine normal male subjects. In six of these subjects, serum hGH also increased after L-dopa treatment. In five untreated acromegalics with high hGH, L-dopa caused inhibition of hGH. APO, like L-dopa, caused a fall in serum hGH in subjects with high growth hormone levels. Both caused comparable suppression of hPRL secretion in subjects with elevated serum prolactin levels, including four patients with pituitary tumors. These results confirm that a central dopamine DA mechanism modulates hGH and hPRL secretion in man. The implications of DA control and stimulation for hyperprolactinemic states is also discussed. (Journal abstract modified)

188838 Kurioka, Yoshiyuki. Hanna Sanatorium, Japan **Effects of chlorpromazine plasma levels on electrocardiogram.** Clinical Psychiatry (Tokyo). 15(9):1001-1009, 1974.

The effect of chlorpromazine (CPZ) plasma levels on electrocardiogram is studied, based on an experiment in which 11 23-33-year old male and 11 18-45-year-old female schizophrenics were orally treated with CPZ, and their CPZ plasma levels and electrocardiographic changes were examined. It was found that the CPZ level per body weight was greater for females than for males. Electrocardiographic changes were apparent for most Ss. Results indicate that there is a significant correlation between the CPZ plasma level and the occurrence of electrocardiographic change, and the the CPZ plasma levels are significantly influenced by individual and sex differences. Since females showed higher CPZ plasma levels, it is felt that the dose of CPZ should be smaller for females than that for males. 29 references.

189075 Ornston, Darius; Schwartz, Marc; Smith, D. Clint; Stern, Stanley. 255 Bradley Street, New Haven, CT 06510 **Laboratory studies for every medicated outpatient: are they really necessary?** American Journal of Psychiatry. 131(6):711-714, 1974.

Results of a questionnaire distributed to all members of a local psychiatric society concerning usual practice among psychiatrists in regard to laboratory tests are reported. The value of routine blood studies for every patient who takes psychotropic medication is questioned. Generally, routine studies provide little useful information. 12 references. (Author abstract modified)

189595 Muller, W.; Wollert, U. Pharmakologisches Institut der Universitat, D-6500 Mainz, Obere Zahlbacher Str. 67, Germany **Influence of pH on the benzodiazepine-human serum albumin complex: circular dichroism studies.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 283(1):67-82, 1974.

The influence of pH on the binding of benzodiazepine derivatives to human serum albumin (HSA) was studied by circular dichroism measurements and by gel filtration. The binding of nearly all benzodiazepines is increased by rising the pH from 6.60 to 8.20. For flurazepam, clonazepam, and nitrazepam this increase in binding is due to an increase of the affinities, while for the other substances the affinity remains constant and the number of binding sites is increased from one to two. The changes in binding of the benzodiazepines by rising the pH are explained by a cationic amino acid residue near or at the benzodiazepine binding site of the HSA molecule. This second binding site is not detectable by circular dichroism. For several of the substances, rising the pH from 6.60 to 8.20, is accompanied by large alterations of the optical properties of the HSA benzodiazepine complexes. These alterations are explained by changes of the asymmetric environment of the benzodiazepine binding site at the HSA molecule in the structural transition at slightly alkaline pH values. 31 references. (Author abstract)

189734 Lipper, Steven. Neurological Unit, Boston State Hospital, 591 Morton St., Boston, MA 02124 **Impairment of optokinetic nystagmus in patients with tardive dyskinesia.** Archives of General Psychiatry. 28(3):331-333, 1973.

Fifteen chronic psychiatric patients who had received psychotropic drugs for at least 10 years and who were diagnosed as having tardive dyskinesia were tested with a control group, for optokinetic nystagmus. Results were that impaired or absent optokinetic nystagmus was observed significantly more frequently among patients with tardive dyskinesia than among nondyskinetic control subjects. It is concluded that, in view of known abnormal ocular motor responses in patients with Parkinson disease and Huntington chorea, this finding may be a consequence of chronic chemical denervation of dopamine receptors in the striatum. 16 references. (Author abstract modified)

189903 no author. no address **John J. Bonica on pain management.** Hospital Physician. 10(8):22-28, 1974.

An interview with John J. Bonica examines management of pain, and brief reports by Bonica deal with the mechanisms of pain and pain clinics. Stress is given to the need for a thorough medical history to diagnose the cause of pain. Nerve blocks in diagnosing and treating pain are discussed, and surgical and medical treatments are examined. It is noted that for mild to moderate pain, it is best to start with nonaddictive drugs, which include the salicylates, salicylamide, the aniline derivatives, the phenylpyrazoles, mefenamic acid (Ponstel), and indomethacin (Indocin). Of these, aspirin is still the best and most widely used because it is effective and inexpensive and has few side-effects.

189923 Crane, George E.; Smeets, Ronald A. Spring Grove State Hospital, Department of Mental Hygiene, Baltimore, MD 21228 **Tardive dyskinesia and drug therapy in geriatric patients.** Archives of General Psychiatry. 30(3):341-343, 1974.

Tardive dyskinesia is related to the total intake of neuroleptics. The data were based on a selected sample of geriatric patients, on accurate and complete information on chemotherapy, and on three neurological examinations. A seven point rating scale was used to distinguish drug induced from spurious motor abnormalities. Two statistical approaches demonstrated that the risk of oral dyskinesia increases with the exposure to neuroleptics. 5 references. (Journal abstract modified)

190104 Parker, D. C.; Rossman, L. G.; Siler, T. M.; Rivier, J.; Yen, S. S. C.; Guillemin, R. Room 6051, VA Hospital, La Jolla, CA 92037 **Inhibition of the sleep-related peak in physiologic human growth hormone release by somatostatin.** Journal of Clinical Endocrinology and Metabolism. 38(3):496-499, 1974.

The capability of somatostatin to completely suppress physiologically maximal human growth hormone (hGH) release in early sleep of four normal subjects and to diminish nocturnal release in one acromegalic is reported. The synthetic linear tetradecapeptide, somatostatin, was given over the first 90 min of sleep on two nights to each of four normal young men and on one night to an acromegalic patient. Complete inhibition of the sleep related physiologic peak in nychthemeral hGH release was seen during infusion on all eight nights in normal subjects and a 50% reduction was seen in the acromegalic. This occurred without alteration in sleep in the first cycle. Thus, potent somatotrophin release inhibiting factor activity in physiologic and pathologic hGH retease was exhibited by somatostatin. 10 references. (Author abstract modified)

190147 Zsigmond, Elemer K.; Flynn, Kathy; Martinez, Orestes A. Univ. of Michigan Medical Center, Dept. of Anesthesiology, Ann Arbor, MI 48104 **Diazepam and meperidine on arterial blood gases in healthy volunteers.** Journal of Clinical Pharmacology. 14(7):377-381, 1974.

Diazepam and meperidine effects on arterial blood gases in healthy volunteers are reported. Arterial blood gases were not significantly altered by 0.15 mg/kg I.V. dose of diazepam in volunteers. The PaO2 was significantly reduced and the PaCO2 increased following administration of meperidine 1.5mg/kg with diazepam 0.15 mg/kg. Diazepam did not significantly increase the respiratory depression induced by meperidine. Values for arterial pH were not significantly affected in any of the groups. 10 references. (Author abstract modified)

190314 Fann, W. E.; Lake, C. R.; Gerber, C. J.; McKenzie, G. M. Department of Psychiatry, Baylor College of Medicine, 1200 Moursund Avenue, Houston, TX 77025 **Cholinergic supression of tardive dyskinesia.** Psychopharmacologia (Berlin). 37(2):101-107, 1974.

The hypothesis that tardive dyskinesia (TD), a hyperkinetic disorder associated with long-term neuroleptic treatment, may be a manifestation of imbalance of opposing DA and ACh dependent systems in the CNS (i.e.,hyperdopamine activity or hypocholinergic function) was tested. Dopamine blocking agents give some transient relief of symptoms. Physostigmine, an anticoholinesterase which enhances central nervous system acetylcholine action, was given to seven subjects with TD and measurements of their pathological movements were made before, 45 min and 24h later. All seven subjects showed significant suppression of movement at 24h. Many showed measurable decrement at 45 min. Side-effects were minimal and transient. It is concluded that physostigmine suppresses movements of TD. 15 references. (Author abstract)

191096 Siris, J. H.; Pippenger, C. E.; Werner, W. L.; Masland, R. L. Section of Neurological Services, Creedmoor State Hospital, 80-45 Winchester Blvd., Queens Village, NY

Anticonvulsant drug-serum levels in psychiatric patients with seizure disorders: effects of certain psychotropic drugs. New York State Journal of Medicine. 74(9):1554-1556, 1974.

The effect of chronic administration of chlorpromazine, diazepam, and thioridazine on serum anticonvulsant drug levels was studied in 24 hospitalized patients with psychiatric and major motor seizure disorders. Results demonstrate that serum diphenylhydantoin (DPH) levels are significantly altered in some patients receiving any one of these three psychotropic drugs along with DPH and phenobarbital, when compared with a control group receiving only DPH and phenobarbital. 15 references. (Author abstract modified)

191233 Malarkey, William B.; Cyrus, Jahangir; Paulson, George W. Dept. of Medicine, Ohio State Univ. Hospitals, Columbus, OH 43210 **Dissociation of growth hormone and prolactin secretion in Parkinson's disease following chronic L-dopa therapy.** Journal of Clinical Endocrinology and Metabolism. 39(2):229-235, 1974.

Growth hormone (GH) and prolactin (PRL) secretion during a 24 hour period is reported after evaluation of 10 patients with Parkinson's disease, who had ingested 2-5g of L-dopa per day for 2.5to 4 years. No patient displayed clinical evidence of acromegaly, and mean concentration of GH over a 24 hour period was normal. L-dopa failed to stimulate GH secretion 79% of the time in these patients. Only one patient consistently demonstrated a GH secretory peak after each dose of L-dopa given during a 24 hour interval. Further evidence of disturbed GH regulation is reported. In all patients, serum PRL was appropriately suppressed by L-dopa. A normal nocturnal PRL secretory peak was observed in all but one patient. It is concluded that mean concentration was not excessive in these patients; however, individual 24 hour GH doses of L-dopa produced a variable secretory response in contrast to uniform suppression of serum prolactin following chronic L-dopa therapy. 31 references. (Author abstract modified)

191444 Ehrnebo, M. Central Military Pharmacy/Karolinska Pharmacy, Karolinska Hospital S-10401 Stockholm 60, Sweden **Pharmacokinetics and distribution properties of pentobarbital in humans following oral and intravenous administration.** Journal of Pharmaceutical Sciences. 63(7):1114-1118, 1974.

The pharmacokinetics of intravenously and orally administered pentobarbital were studied in humans by gas chromatography (GC) analysis of plasma and the data were simulated with the aid of digital computation. The drug had an apparent disposition half-line of 22.3plus/minus 4.0(SD) hr when administered intravenously to seven healthy Ss and after oral doses the half-line was about the same. An examination of the individual pharmacokinetic constants showed that the volume of the peripheral compartment in the two compartment open model appeared to increase bodyweight in the Ss. This influenced the tissue to central compartment distribution of the drug. Formulae are presented which allow calculation of fractions of amount in the central compartment distributed to plasma water, plasma proteins, blood cells and associated fluid. The application of these equations shows that of the total amount in the central compartment about 87% is in the associated fluid: of the 13% in the systemic circulation, 4% is in plasma water, 5% is bound to plasma proteins and the other 4% is distributed to blood cells. It is concluded that pentobarbital exhibits extensive tissue binding. 14 references. (Author abstract modified)

191502 Murphy, Dennis L.; Donnelly, Cynthia. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD **Monoamine oxidase in man: enzyme characteristics in human platelets, plasma, and other human tissues.** Psychopharmacology Bulletin. 10(3):10-11, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, available information on substrate, inhibitor, and electrophoretic characteristics of the monoamine oxidases (MAO) in human platelet, plasma, and brain and liver tissue was summarized. The data indicate that two or more multiple forms of MAO exist in human brain and liver, while human platelets apparently contain only one form which manifests many substrate and inhibitor related characteristics that are similar to those of mitochondrial MAO's found in other tissues. In contrast, human plasma MAO is a distinctly different enzyme with different substrate and inhibitor related responses, and plasma MAO activity is not correlated with platelet MAO activity. A large genetic influence on individual differences in both platelet and plasma enzyme activities exists. Except for MAO inhibiting drugs, most psychoactive drugs have minimal effects on platelet MAO activity.

191506 Meltzer, H. Y.; Sachar, E. J.; Frantz, A. G. Department of Psychiatry, University of Chicago Pritzker School of Medicine, Chicago, IL **Serum prolactin levels in newly admitted psychiatric patients.** Psychopharmacology Bulletin. 10(3):14-15, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a study was described which tested the hypothesis that excessive dopaminergic activity may be involved in the etiology of some types of schizophrenia. Serum prolactin levels in newly admitted, unmedicated psychiatric patients were determined to find whether the prolactin levels in schizophrenic patients were diminished to reflect increased dopaminergic activity in the tuberoinfundibular tract or the increases associated with psychological stress. Mean serum prolactin concentration was within the normal range in 22 acutely disturbed newly admitted schizophrenics, but was elevated in two manic patients and in one patient with a severe anxiety state. Second samples obtained 1-3 days later in 10 schizophrenics had significantly greater mean prolactin concentration than the initial sample. Results indicate a probable balance between the stimuli to increased prolactin secretion due to stress and to decreased prolactin secretion due to dopaminergic hyperactivity, rather than the absence of both stimuli. Four phenothiazines, including thioridazine, raised serum prolactin levels equivalently in these Ss, most likely due to their blockade of dopamine receptors. 9 references.

191507 Angrist, Burton M.; Gershon, Samuel. New York University Medical Center, New York, NY **Dopamine and psychiatric states: preliminary remarks.** Psychopharmacology Bulletin. 10(3):15, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, problems in clarifying the precise mechanisms involved in the observed role of dopamine in some psychotic states were discussed. Such a role is suggested by the relationships among the stimulant psychoses and their treatments, stereotyped behavior and its antagonism, and the biochemical pharmacology of neuroleptics and their association with extrapyramidal side-effects. Some problematic inconsistencies may relate to: differing effects on dopaminergic systems in different anatomical sites; specific mechanisms by which synaptic activity is either enhanced or diminished; or relationships between dopaminergic activity and that of other

neurotransmitters. However, this does not diminish the role of dopamine in psychotogenesis. Rather, the resolution of these inconsistencies may lead to a more precise understanding of the mechanisms involved in this provocative hypothesis.

191510 Goldstein, M.; Freedman, L. S.; Ebstein, R. P.; Park, D. H.; Kashimoto, T. New York University Medical Center, Department of Psychiatry, Neurochemistry Laboratories, New York, NY **Human serum dopamine-beta-hydroxylase: relationship to sympathetic activity in physiological and pathological states.** Psychopharmacology Bulletin. 10(3):25, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the relationship between human serum dopamine-beta-hydroxylase (DBH) and sympathetic activity in physiological and pathological states was reported. In an attempt to determine factors involved in reliable clinical interpretation of serum DBH levels, human serum DBH activity and immunoreactive IR-DBH levels were determined in various physiological and pathological states; the effect of pressor response in humans on circulatory IR-DBH and on DBH activity was studied; and serum DBH levels were measured in patients with various disorders and in healthy family members. Serum DBH activity and serum IR-DBH levels were significantly lower in Down's syndrome patients than in age matched controls. Serum DBH levels failed to differentiate among patients with various psychiatric disorders, and the values were compatible with those obtained for normal controls. Findings suggest that serum DBH levels can only be reliably interpreted when an evaluation is made of the influence of familial factors in control of basal serum DBH levels or when individual serum DBH levels are monitored serially in longitudinal studies.

191511 Lovenberg, Walter; Bruckwick, Eleanor A.; Alexander, R. Wayne. National Heart and Lung Institute, National Institutes of Health, Bethesda, MD **An evaluation of serum dopamine-beta-hydroxylase as an index of sympathetic nerve activity in man.** Psychopharmacology Bulletin. 10(3):26-27, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the question of whether or not human serum dopamine-beta-hydroxylase (DBH) represents an index of sympathetic nerve activity was discussed. A wide range in the level of serum DBH was found in normal Ss and varied as a result of strenuous physical activity or lack of it. No significant correlation of DBH with hypertension was noted, although Black Ss had lower mean activity than Whites, a finding contradictory to those of other research. Measurement of serum levels of DBH in patients with several diseases thought to involve alterations in norepinephrine synthesis revealed that such activity is normal in schizophrenia and manic-depressive illness, somewhat reduced in dysautonomia and Down's syndrome, and somewhat elevated in torsion dystonia, Huntington's chorea, neuroblastoma, and pheochromocytoma. It is concluded that considerable caution must be exercised when serum DBH activity is used as an index of sympathetic activity; this enzyme does not appear to be an unambiguous marker for any disease state. 18 references.

191512 Schanberg, Saul M.; Stone, Richard A.; Kirshner, Norman. Duke University Medical Center, Durham, NC 27706 **Serum dopamine-beta-hydroxylase: a possible aid in the evaluation of hypertension.** Psychopharmacology Bulletin. 10(3):27-28, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, results were reported of a test of whether or not dopamine-beta-hydroxylase (DBH) activity may be useful in evaluation of patients with hypertension. Plasma DBH concentration was determined in 50 consecutive patients with hypertension and results suggest that plasma DBH activity falls within a narrow range in young adults with normal stable blood pressure. Its measurement may aid in the evaluation and understanding of certain forms of hypertension. 2 references.

191522 Lieberman, Abraham; Le Brun, Yves; Boal, Dinkar; Zolfaghari, Mehdi. Department of Neurology, New York University School of Medicine, New York, NY **Effects of piribedil (ET 495) -- a dopaminergic receptor stimulating agent in Parkinson's disease.** Psychopharmacology Bulletin. 10(3):42-43, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the effects of piribedil (ET 495), a dopaminergic receptor stimulating agent with properties resembling apomorphine, in Parkinson's disease were discussed. Relief of tremor, when it occurred, was more pronounced after parenteral (intravenous) administration of piribedil in dosages of 0.05mg/kg. Parenteral administration in man was limited by development of vomiting, an effect not observed in the monkey. The effects of piribedil may be mediated by a metabolite and a catechol bearing a close resemblance to dopamine. This compound, like dopamine, is unable to penetrate the blood-brain barrier, and the antiparkinsonian effects of piribedil may depend on the ability of the drug to avoid being metabolized in the periphery, to penetrate the blood-brain barrier, and to be converted to the metabolite. 10 references.

191524 Chase, Thomas N. Neurology Unit, NIMH, Bethesda, MD **Clinical studies of dopaminergic mechanisms.** Psychopharmacology Bulletin. 10(3):43-44, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, the mechanism of the antiparkinsonian action of L-DOPA was described, by comparing the clinical effects of L-DOPA with those of a presumptive direct acting dopamine (DA) receptor. DA turnover was estimated by the rate of homovanillic acid (HVA) increase in lumbar cerebrospinal fluid following the oral administration of probenecid in one experiment. The therapeutic efficacy and toxicity of orally administered piribedil was compared against an inert placebo in 16 patients with idiopathic parkinsonism in another, as well as against the effects of L-DOPA. Overall results indicate that the percent improvement with piribedil is independent of the pretreatment severity of parkinsonian signs. Conceivably, the drug serves as only a partial DA receptor agonist or presynaptic effects contribute to its ability to modify DA mediated function. Pharmacokinetic factors or the ability of piribedil, as well as L-DOPA, to influence monoaminergic systems other than those containing DA may also explain the results. Although the antiparkinsonian efficacy of piribedil approximates that of conventional anticholinergic preparations, it is thought unlikely that the drug acts primarily as a central cholinolytic agent.

191529 Wise, C. David; Stein, Larry. Wyeth Laboratories, Philadelphia, PA **Post-mortem measurement of enzymes in human brain: evidence of a central noradrenergic deficit in schizophrenia.** Psychopharmacology Bulletin. 10(3):48-49, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, a neurochemical model of schizophrenia was proposed which predicts evidence of a central noradrenergic deficit in schizophrenia, as indicated by postmortem measurement of enzymes in the human brain. It was posited that the noradrenergic reward pathways and their rich terminal systems in diencephalon and limbic forebrain are sites of critical damage. Findings from the postmortem studies indicate: (1) deficits in dopamine-beta-hydroxylase (DBH), the enzyme responsible for the final step in norepinephrine biosynthesis; (2) observed reduction in catechol-O-methyl transferase (COMT), providing information about the postsynaptic component of noradrenergic systems and consistent with observed DBH deficits; (3) significant reduction in choline acetyltransferase (CAT) activity in the hippocampus, pons-medulla, and diencephalon, providing both biochemical and physiological evidence of the role of the central noradrenergic deficit in schizophrenia; and (4) lack of differences between normal and schizophrenic groups in the activities of lactate dehydrogenase, monoamine oxidase, and superoxide dismutase, making it unlikely that gross artifacts are responsible for the observed enzymatic deficits. 2 references.

191536 Frohman, C. E.; Caldwell, D. F.; Gottlieb, J. S. Lafayette Clinic, Detroit, MI **Abnormalities in tryptophan metabolites in schizophrenia.** Psychopharmacology Bulletin. 10(3):56-57, 1974.

At the Twelfth Annual Meeting of the American College of Neuropsychopharmacology held in Palm Springs, California in December, 1973, results were reported of experiments conducted to determine if excess of tryptophan in humans and animals would affect tryptophan metabolism and subsequently lead to symptoms which might resemble schizophrenia. Freshly obtained bovine hypothalamus was incubated with both the helical and nonhelical forms of the S protein and tryptophan. After 1 hour, levels of methylated tryptophan metabolites were measured by gas chromatography. A significant increase in DMT was found in samples incubated with alpha-helical protein and not in those with the nonhelical protein. Tests with schizophrenic patients and controls given a load of 5g tryptophan per day for 14 days indicated DMT presence in urine of schizophrenics but not in controls, and excretion was also increased in urine of loaded schizophrenics but not in loaded controls. The helical form of the S protein caused a degree of anhedonia in rats with electrodes implanted in the median forebrain bundle. There is a possibility that the decrease in stimulation rate in rats given the helical form of the S protein resulted from excess DMT formation in the brain. 2 references.

191625 Koshino, Yoshifumi; Otsuka, Royosaku. Department of Neuropsychiatry, Kanazawa University, Japan **Psychotropic drugs and electroencephalography -- first report.** Clinical Electroencephalography (Osaka). 16(1):55-64, 1974.

The literature on the influence of psychotropic drugs on human EEG is reviewed. The influence of single injection intravenous or intramuscular administration and chronic oral administration of chlorpromazine on human EEG is considered. The abnormal EEG of two females who had received excessively large doses of chlorpromazine as treatment for attempted suicide is also dicussed. 31 references.

191667 Koshino, Yoshifumi; Otsuka, Ryosaku. Department of Neuropsychiatry, Kanazawa University, Japan **Psychotropic drugs and electroencephalography -- second report.** Clinical Electroencephalography (Osaka). 16(2):117-128, 1974.

The literature on the influence of psychotropic drugs on human EEG is reviewed. The influence of antianxiety agents, such as meprobamate, levomepromazine, thioridazine, perphenazine, haloperidol, and chlorprothixene on EEG is considered. The influence of antidepressants, such as imipramine, amitriptyline, clomipramine and MAO inhibitors on EEG is also discussed. 56 references.

191770 Gaut, Zane N. Dept. of Biochemical Nutrition, Hoffmann-La Roche, Inc., 340 Kingsland, Street, Nutley, NJ 07110 **Influence of various substances which induce and inhibit aggregation on the uptake of deoxyglucose by human blood platelets.** Journal of Pharmacology and Experimental Therapeutics. 190(1):180-186, 1974.

Substances which inhibit human blood platelet aggregation, including cyproheptadine, phenothiazines, and tricyclic antidepressants suppressed deoxyglucose uptake, whereas substances which promote platelet aggregation, such as serotonin, epinephrine, norepinephrine, adenosine diphosphate, and thrombin increase uptake. Cyproheptadine produced a similar inhibition of deoxyglucose uptake in the presence and in the absence of norepinephrine or serotonin. Hence, such inhibition by substances which suppress aggregation and stimulation by substances which promote aggregation may be related to their effects on platelet functions. The lack of influence by various antiinflammatory drugs at 0.5mM suggests that their inhibition of aggregation embodies a different mechanism than inhibition of glucose uptake. The possible relationships between inhibition of glucose uptake and the hyperglycemic reactions in humans to these drugs are discussed. 43 references. (Author abstract modified)

191924 Biggs, John T.; Sherman, William R. Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110 **Protriptyline steady state plasma levels in man.** Pharmacologist. 16(2):219, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, protriptyline steady state levels in man were reported. Patients treated with 10-70mg/day of protriptyline had plasma levels of 170ng/cc. The higher blood levels of protriptyline as compared to nortriptyline may be the result of different metabolism of the two drugs and may account for the activating properties seen when protriptyline is used to treat retarded depressions. (Author abstract modified)

191961 Petersen, B. H.; Graham, J.; Lemberger, L.; Dalton, B. Lilly Laboratory for Clinical Research, Indianapolis, IN 46202 **Studies of the immune response in chronic marihuana smokers.** Pharmacologist. 16(2):259, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, chronic marihuana smokers and matched nonsmokers were compared with respect to several aspects of their immune system. Immunoglobulin production, hemolytic complement levels, response to mitogenic stimulation, the lymphocyte T and B-cell ratios, and phagocytic activity, using polymorphonuclear leucocytes (PMN), were examined. Blood chemistries (SMA 12) and hematologic studies were evaluated. Immunoglobulin (IgG,M,A) and complement levels, SMA 12, and hematologic values from smokers did not appear to differ significantly from those obtained from nonsmokers. Differences were observed; notably, the number of T-cells with respect to the T and B cell ratio was lowered in smokers, and phytohemagglutinin stimulation of lymphocytes was apparently less effective in smokers. The most striking difference between smokers and nonsmokers was observed in their phagocytic capability. Preparations from

smokers contained fewer PMN capable of phagocytizing yeast cells. (Author abstract modified)

192065 Escobar, Javier I.; Schiele, Burtrum C.; Zimmermann, Robert. Department of Psychiatry, University of Minnesota, St. Paul-Ramsey Hospital and Medical Center, 640 Jackson St., St. Paul, MN 55101 **The tranylcypromine isomers: a controlled clinical trial.** American Journal of Psychiatry. 131(9):1025-1026, 1974.

The plus and minus isomers of tranylcypromine were tested under double-blind conditions on 11 depressed patients. Findings indicate that the (-) isomer is the more effective and produces fewer side-effects. Because the (-) isomer has been shown to be a stronger blocker of the reuptake mechanism for brain amines and a weaker inhibitor of monoamine oxidase than the isomer, it is suggested that these results are of particular interest. 8 references. (Author abstract modified)

192420 Theobald, W.; Buch, O.; Delini-Stula, A. Research Laboratories, Ciba-Geigy, S. A., Basel, Switzerland **Correlation of pharmacological investigations with the clinical efficacy of antidepressant drugs.** Activitas Nervosa Superior (Praha). 16(1):54-56, 1974.

The correlation of pharmacological tests with the clinical efficacy of antidepressant drugs was studied with tricyclic drugs. Individual pharmacological effects make it possible to select substances with imipramine like activities. In comparison with desipramine, less accentuation of adrenergic potentiation and a greater atropine like and sedative effects were seen. Amitriptyline possesses pronounced cholinolytic and central depressant effects. Trimeprimine and opipramol show only a slight accentuation of adrenergic and serotoninergic function. 16 references.

192428 Ehlers, W.; Huber, H. P. Psychological Department, University of Dusseldorf, Dusseldorf, Germany **The effects of Hoe 36 801 on catecholamine excretion, heart rate and psychomotor performance in neurotics and normals.** Activitas Nervosa Superior (Praha). 16(1):70-71, 1974.

The effects of Hoe 36 801 on biochemical and psychophysiological indicators of activation were studied in rats. The data indicated no statistically significant effects on psychomotor performance in peg board, tapping and pursuit rotor. The data revealed significant effects on adrenaline excretion in neurotics and normals. Heartrate in rest was found to remain invariant under the influence of the drug. 7 references.

192511 Shoshkes, Milton. 116 Millburn Ave., Summit, NJ **The use of propranolol with various drug combinations in the treatment of essential hypertension.** Journal of the Medical Society of New Jersey. 71(8):581-583, 1974.

Seventeen ambulatory hypertensive patients who had been unresponsive to standard antihypertensive therapy with drug combinations, supplemented by strict dietary salt restrictions, were treated with the addition of oral propranolol in dosages of 40 to 160 mg daily. This beta-adrenergic blockage therapy was found to have a superior blood pressure lowering effect in 15 out of 17 patients, and it was uniquely free of side-effects. It is concluded that propranolol is a valuable addition in the combined antihypertensive therapy with multiple drugs. 2 references. (Author abstract)

192575 Clifford, John M.; Cookson, James H.; Wickham, Phyllis E. G. D. Searle & Co., Lane End Rd., High Wycombe, Bucks., HP12 4HL England **Absorption and clearance of secobarbital, heptabarbital, methaqualone, and ethinamate.** Clinical Pharmacology and Therapeutics. 16(2):376-389, 1974.

The absorption and clearance of secobarbital, heptabarbital, methaqualone, and ethinamate were studied by measurements of blood and plasma drug levels after single oral dosage in the therapeutic range to nonfasting subjects. Determinations of blood and plasma levels were carried out to the limits of sensitivity of the gas - liquid chromatographic determination steps. The mean maximum plasma level of ethinamate was observed after 1 hour; that of methaqualone occurred after 2 hours; the mean maximum blood level of secobarbital was found after 3 hours; whereas that of heptabarbital was not observed until the sixth hour. Secobarbital was cleared slowly from the blood. Secobarbital, heptabarbital, and methaqualone could all be detected in the body 24 hours after they had been given. Half-lives were also calculated. 36 references. (Author abstract)

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187257 Mendelson, Jack H.; Rossi, A. Michael; Bernstein, Jerrold G.; Kuehnle, John. Department of Psychiatry, Harvard Medical School, Boston, MA **Propranolol and behavior of alcohol addicts after acute alcohol ingestion.** Clinical Pharmacology and Therapeutics. 15(6):571-578, 1974.

Sixty four adult male chronic alcoholic addicts were studied to assess the effects of propranolol pretreatment on behavioral changes induced by acute ingestion of alcohol. Research ward conditions were controlled and a double-blind technique was employed. Pretreatment with 10, 20, and 40mg of propranolol four times a day for 3 consecutive days prior to alcohol administration failed to block or attenuate cognitive, perceptual, motor, and affective changes induced by acute alcohol intoxication. 24 references. (Author abstract)

187581 Werry, John S.; Sprague, Robert L. Dept. of Psyhiatry, University of Auckland School of Medicine, Auckland, New Zealand **Methylphenidate in children -- effect of dosage.** Australian and New Zealand Journal of Psychiatry (Carlton). 8(1):9-19, 1974.

The effect of dosage on methylphenidate treatment in children was studied in a clinical trial of two groups of hyperactive aggressive children. It was found that methylphenidate was superior to placebo for about two thirds of the children, but there was little difference in effectiveness between different dosage levels, especially once 0.3mg/kg is attained. Mild side-effects were common at higher dosages. Evaluation of a variety of physician, parent, teacher, psychological test and behavioral measures revealed the greater sensitivity of teacher and physician ratings to drug effects. No measures, including neurological ones, discriminated between responders and nonresponders. Results suggest that methylphenidate is a useful treatment for hyperactive aggressive children, but current doses may be too high and side-effects more common than stated. 26 references. (Author abstract modified)

187642 Post, R. M.; Gillin, J. C.; Wyatt, R. J.; Goodwin, F. K. 3-West Clinical Research Unit, NIMH, Bldg. 10, Room 3S239, 9000 Rockville Pike, Bethesda, MD 20014 **The effect of orally administered cocaine on sleep of depressed patients.** Psychopharmacologia (Berlin). 37(1):59-66, 1974.

Cocaine was administered orally on a double-blind basis to depressed patients and effects on EEG monitored sleep were assessed. In doses which did not produce consistent effects on

vital signs or mood, cocaine significantly reduced total sleep and rapid eye movement (REM) sleep. The REM sleep supression with cocaine administration and rebound upon cocaine discontinuation was dose related; there was a greater effect at higher doses. Two properties of cocaine appear to closely correspond to those of many other drugs which suppress REM sleep in man -- enhancement of functional catecholamines and/or high drug abuse potential. 45 references. (Author abstract).

187929 Freemon, Frank R. Neurology Service, Veteran's Hospital, 1310 24th Avenue South, Nashville, TN 37203 **The effect of delta9-tetrahydrocannabinol on sleep.** Psychopharmacologia (Berlin). 35(1):39-44, 1974.

In an examination of the effect of delta9-tetrahydrocannabinol (THC) on sleep, five volunteers slept 8 to 15 consecutive nights in the laboratory with electroencephalogram, chin electromyogram, and eye movements monitored by the Dement and Kleitman method. THC, 20mg administered at bedtime, decreased the amount of time spent in the rapid eye movement (REM) or paradoxical phase of sleep. Abrupt withdrawal of THC after 4 to 6 consecutive nights of use produced a mild insomnia characterized by difficulty in falling and staying sleep but did not produce a marked REM rebound. 9 references. (Author abstract)

188226 Wright, Dennis C. Dept. of Psychology and Dalton Research Center, University of Missouri, Columbia, MO 65201 **Differentiating stimulus and storage hypotheses of state-dependent learning.** Federation Proceedings. 33(7):1797-1799, 1974.

The possible separation of the stimulus effects of a drug from the effects of that drug on memory storage and retrieval was studied, suggesting that state dependent learning can occur in the absence of drug stimulus effects during learning. Two experiments are discussed in which acquisition training drug states were induced immediately after completion of the training trial. Since drug effects were absent in the stimulus sampling and response intervals during training but were present in the memory storage interval immediately following training, the predictions of the storage and stimulus hypotheses could be contrasted. Storage hypothesis predictions of retention test performance were confirmed and stimulus hypothesis predictions were not. The suggestion was made that experimenters using posttraining administration of 'amnesic' agents should examine the possibility that they are studying memory retrieval failure rather than memory storage failure. 8 references. (Author abstract modified)

188542 Janowsky, David S.; El-Yousef, M. Khaled; Davis, John M. Department of Psychiatry, University of California at San Diego, School of Medicine, La Jolla, CA 92037 **Acetylcholine and depression.** Psychosomatic Medicine. 36(3):248-257, 1974.

Physostigmine, a cholinesterase inhibitor which increases central acetylcholine levels, has been found to increase depressed mood in patients with an affective component to their symptoms (manics, depressives, and schizoaffectives). Schizophrenics without an affective component did not become depressed. After physostigmine administration, all subject groups showed a significant increase in symptoms including lethargy, slowed thoughts, withdrawal, apathy, decreased energy, and motor retardation, indicating a state of psychomotor retardation, and all became less cheerful and talkative. Results are compatible with the hypothesis that acetylcholine may be involved in the etiology of affective disorders. 17 references. (Author abstract modified)

189043 Firth, Hugh. Dept. of Psychology, Univ. of Liverpool, Liverpool, England **Sleeping pills and dream content.** British Journal of Psychiatry (London). 124:547-553, 1974.

The effects of amylobarbitone and nitrazepam on dream content were studied through assessments of experienced judges and subjective estimates in 20 subjects who spent from seven to 11 nights in the laboratory. Contrary to prediction, dreams were virtually indistinguishable before, during, and after chronic administration of either of the two drugs or placebo. Two effects were that nitrazepam made dreams take on an ordinary, every day characteristic, and its withdrawal made them bizarre; and withdrawal of amylobarbitone produced exceptionally vivid dreams and nightmares at home but not in the laboratory. Results suggest that these hypnotics affect the quality of the thought processes in sleep, and in clinical use their withdrawal may produce unpleasant, anxiety filled dreams and nightmares. 35 references. (Author abstract modified)

189358 Moskowitz, Herbert; Shea, Richard; Burns, Marcelline. Psychology Department, University of California, Los Angeles, CA 90024 **Effect of marihuana on the psychological refractory period.** Perceptual and Motor Skills. 38(3,Part1):959-962, 1974.

Reaction times to an auditory stimulus (RT1) and a subsequent visual stimulus (RT2) were measured for 12 Ss under three levels of smoked marihuana. Marihuana impaired responses; effect was larger on RT2 than on RT1. However, delays of RT2 are longer than would be predicted in terms of the psychological refractory period. 4 references. (Author abstract)

189359 Sharma, Satanand; Moskowitz, Herbert. University of California, Irvine, CA 02664 **Effects of two levels of attention demand on vigilance performance under marihuana.** Perceptual and Motor Skills. 38(3,Part1):967-970, 1974.

The effects of two levels of attention demand on vigilance performance under marihuana were studied. Ss under marihuana performed a modified version of the Mackworth clock vigilance task with two levels of attention and response demands. Similar continuous declines in signal detections over time were found for both experimental conditions indicating that the vigilance decrements induced by marihuana are unrelated to arousal level. 2 references. (Author abstract)

189406 Darley, C. F.; Tinklenberg, J. R.; Roth, W. T.; Atkinson, R. C. VA Hospital, 3801 Miranda Avenue, Palo Alto, CA 94304 **The nature of storage deficits and state-dependent retrieval under marihuana.** Psychopharmacologia (Berlin). 37(2):139-149, 1974.

To explore the nature of the storage deficit produced by marihuana intoxication and to determine if retrieval is state dependent for this drug, 48 subjects were presented 10 20 word lists before receiving an oral dose of marihuana and another 10 lists following drug administration. Subjects studied half of each set of 10 predrug and 10 postdrug lists using an overt fixed rehearsal procedure and half using their normal covert free rehearsal procedure. On day 1 of the experiment an immediate recall test followed each of the 20 lists presented. The marihuana induced deficit in immediate recall performance on day 1 for free rehearsal lists was not eliminated when the fixed rehearsal procedure was used. Marihuana intoxication impaired the storage of information even when overt rehearsal in the drug and no drug states was equated. Three days later (day 4) subjects returned, half receiving marihuana (drug group) and half receiving placebo (placebo group). All subjects

were then administered delayed recall, recognition, and order tests on the words presented on day 1. Delayed recall performance was asymmetrically state dependent, whereas delayed recognition performance was not state dependent. 18 references. (Author abstract)

189408 Landauer, Ali A.; Pocock, Derek A.; Prott, F. W. Department of Psychology, University of Western Australia, Nedlands 6009, Australia **The effect of medazepam and alcohol on cognitive and motor skills used in car driving.** Psychopharmacologia (Berlin). 37(2):159-168, 1974.

The effect of medazepam and alcohol on cognitive and motor skills used in car driving was studied. Questionnaires, motor skill and cognitive tests were given to three groups of 12 healthy young men after administration of either 0, 10 or 20 mg of medazepam (Nobrium). Tests were given both before and after experimental intoxication with 1ml/kg bodyweight of diluted ethanol. On most tests medazepam did not interact with alcohol: no synergistic or antagonistic drug reaction was observed. A greater subjective fatigue rating by the drug groups was not confirmed by objective measures. The use of psychoactive drugs with ambulant patients is discussed and it is concluded that medazepam medication has no detrimental effect on driving ability. 13 references. (Author abstract)

189619 Linnoila, M.; Hakkinen, S. Department of Pharmacology, Siltavuorenpenger 10, Helsinki 17, SF-00170, Finland **Effects of diazepam and codeine, alone and in combination with alcohol, on simulated driving.** Clinical Pharmacology and Therapeutics. 15(4):368-373, 1974.

The effects of single oral doses of codeine, diazepam (Valium), and alcohol on simulated driving were investigated by using a modification of the English Sim-L-car. The driving time was 40 minutes, subjects were told to adapt speed to surroundings and traffic. Placebo increased the inaccuracy of speed estimations. Alcohol increased the numbers of steering wheel reversals and neglected instructions. Diazepam increased the number of collisions and neglected instructions, but the greatest increase in collisions was after codeine. Diazepam generally enhanced the effect of alcohol. 13 references. (Author abstract)

189673 Iswariah, V. St. John's Medical College, Bangalore, India **Some recent hypnotics assessed.** Current Medical Practice (Bombay). 16(7):273-278, 1972.

Some recent hypnotics, including barbiturate and nonbarbiturate hypnotics, tranquilizers, and antihistamines, which are used in the treatment of insomnia are assessed. The report is based on observations of subjects such as medical students, colleagues, household members, neighbors, and friends in India. Findings indicate that most hypnotics tested are effective when taken by mouth on an empty stomach; others, such as quinal barbitonum, glutethamide and buto barbitonum, have a delayed effect or none. Whether the hypnotic caused sleep which was permissive or compulsive was equivocal, except for mandrax, which caused compulsive sleep. Drowsiness as an aftereffect was also equivocal. The desire to repeat was noticed with mandrax, doriden, and to a lesser extent with quinal barbitonum. With the dosage and frequency used in the trial, none of the agents showed any serious side-effects or aftereffects. The physiology of sleep and possible site of action is discussed briefly.

189743 Reiss, David; Salzman, Carl. Room 3N212, 9000 Rockville Pike, NIMH, Bldg. 10, Bethesda, MD 20014 **Resilience of family process: effect of secobarbital.** Archives of General Psychiatry. 28(3):425-433, 1973.

Secobarbital was administered to offspring of family threesomes to test the resiliency of family problem-solving processes to psychological changes in one of its members. Twenty four families were used, half receiving 175mg of secobarbital and the other half receiving a placebo on a double-blind basis. Family problem-solving and speech patterns were measured by a card sorting experimental procedure and computer analysis of automatically transcribed voice records. The drug produced no objective change in the problem-solving of the offspring or his family but produced marked changes in the family's speech patterns. The findings suggest that speech changes may have been compensatory, preventing a sustained change in family problem-solving process in response to the drug. 24 references. (Author abstract)

189884 Feinberg, I.; Hibi, S.; Cavness, C.; March, J. Veterans Administration Hospital, San Francisco, CA 94121 **Absence of REM rebound after barbiturate withdrawal.** Science. 185(4150):534-535, 1974.

It is demonstrated that REM rebound does not regularly ensue after a period of barbiturate induced REM suppression. Administration of three different barbiturates (phenobarbital, amobarbital, and secobarbital) reduced rapid eye movement (REM) sleep; and drug withdrawal led to a return to baseline REM values without significant overshot. Similar results are observed with administration of benzodiazepines in pharmacologically equivalent doses; therefore, a distinction between these two drug classes on the basis of withdrawal effects on the sleep electroencephalogram appears unwarranted. Further investigation is required to determine why high REM levels are sometimes associated with the withdrawal of sedative hypnotic agents. 16 references. (Author abstract modified)

190308 Cohen, Michael J.; Rickles, William H., Jr. VA Hospital, Sepulveda, CA 91343 **Performance on a verbal learning task by subjects of heavy past marijuana usage.** Psychopharmacologia (Berline). 37(4):323-330, 1974.

Human, male subjects (Ss) from a heavy usage category were given paired associate learning in a 2X2 state dependent learning design. No significant effects were found between marihuana and placebo groups on trials to criterion, and recall of the task 7 days later was not found to be state dependent. The results were compared to a previous study using light usage subjects that reported a state dependent effect. The effects Ss marihuana usage history and the drug's acute effects on learning and recall were discussed. 14 refernces. (Author abstract)

190312 Mormont, C. Clinique psychiatrique universitaire, Rue Saint-Laurent, 58 B-4000 Liege, Belgium /**Rating of psychological effects induced by 'ordinary' Noveril and time-released Noveril.**/ Evaluation des effects psychologiques du Noveril simple et du Noveril TR. Psychopharmacologia (Berlin). 37(4):365-370, 1974.

The psychological effects induced by Noveril and time released Noveril were rated. Ratings were made with two depression scales (Hamilton, Breulet), and anxiety scale (Cattell) and Minnesota Multiphasic Personality Iwentory. The results in two groups of depressed inpatients (11 and 9 patients) were examined statistically by the Mann-Whitney Test. The experimental design implied double-blind, crossover and randomization. The two forms of Noveril are found antidepressant but the ordinary Noveril seems more active. 1 references. (Author abstract)

190316 Darley, C. F.; Tinklenberg, J. R.; Roth, W. T.; Atkinson, R. C. VA Hospital, 3801 Miranda Avenue, Palo Alto, CA 94304 **The nature of storage deficits and state-dependent retrieval under marihuana.** Psychopharmacologia (Berlin). 37(2):139-149, 1974.

To explore the nature of the storage deficit produced by marihuana intoxication and to determine if retrieval is state dependent for this drug, 48 subjects were presented 10-20 word lists before receiving an oral dose of marihuana and another 10 lists following drug administration. Subjects studied half of each set of 10 predrug and 10 postdrug lists using an overt fixed rehearsal procedure and half using their normal covert free rehearsal procedure. On Day 1 of the experiment an immediate recall test followed each of the 20 lists presented. The marihuana-induced deficit in immediate recall performance on Day 1 for free rehearsal lists was not eliminated when the fixed rehearsal procedure was used. Thus, marihuana intoxication impaired the storage in information even when overt rehearsal in the drug and no drug states was equated. Three days later (day 4) subjects returned, half receiving marihuana (drug group) and half receiving placebo (placebo group). All subjects were then administered delayed recall, recognition, and order tests on the words presented on day 1. Delayed recall performance was asymmetrically state dependent, whereas delayed recognition performance was not state dependent. 18 references. (Author abstract)

190318 Landauer, Ali A.; Pocock, Derek A.; Prott, F. W. Department of Psychology, University of Western Australia, Nedlands 6009, Australia **The effect of medazepam and alcohol on cognitive and motor skills used in car driving.** Psychopharmacologia (Berlin). 37(2):159-168, 1974.

The effect of medazepam and alcohol on cognitive and motor skills used in car driving was examined. Questionnaires, motor skill and cognitive tests were given to three groups of 12 healthy young men after administration of either 0, 10 or 20mg of medazepam (Nobrium). Tests were given both before and after experimental intoxication with 1ml/kg bodyweight of diluted ethanol. On most tests medazepam did not interact with alcohol: no synergistic or antagonistic drug reaction was observed. A greater subjective fatigue rating by the drug groups was not confirmed by objective measures. The use of psychoactive drugs with ambulant patients is discussed and it is concluded that medazepam medication has no detrimental effect on driving ability. 13 references. (Author abstract)

190321 Haig, John R.; Schroeder, Carolyn S.; Schroeder, Stephen R. Department of Psychology, University of North Carolina, Chapel Hill, NC **Effects of methylphenidate on hyperactive children's sleep.** Psychopharmacologia (Berlin). 37(2):185-188, 1974.

Electroencephalogram sleep patterns recorded from six hyperactive boys taking methylphenidate daily were compared to those of six normal boys. For these hyperactive subjects significant increases in latency to both sleep onset and the first rapid eye movement (REM) period were obtained. Other sleep measures were normal. The hypothesis that the therapeutic effects of stimulants upon hyperactive children are independent of any pathological disruption of sleep was supported. 17 references. (Author abstract)

190743 Regina, Edmund G.; Smith, Gene M.; Keiper, Charles G.; McKelvey, Robert K. Massachusetts General Hospital, Boston, MA 02114 **Effects of caffeine on alertness in simulated automobile driving.** Journal of Applied Psychology. 59(4):483-489, 1974.

The effects of caffeine on four indices of performance in an automobile driving simulator were examined. Initial and supplemental doses of caffeine significantly enhanced performance beyond that found with placebo on four measures of alertness. 7 references. (Author abstract modified)

191137 Lapierre, Y. D. Pierre Janet Hospital, Hull, Quebec, Canada **The comparative anxiolytic effects of placebo, imipramine and chlorimipramine using psychiatric and psychophysiological measurements.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):16-22, 1974.

The anxiolytic properties of imipramine, chlorimipramine and placebo were determined before these drugs acted on anxiety via their antidepressant effect, i.e. during the first week of their administration. It was found that the Max Hamilton Anxiety Rating Scale was not sufficiently sensitive to discriminate any difference between the three groups, if such exists, after 48 hours and after 7 days. The Anxiety Symptom checklist was found to be slightly more discriminative as it did show a tendency for the imipramine group to be less symptomatic. 10 references. (Journal abstract modified)

191138 Ban, T. A.; Lehmann, H. E.; Amin, M.; Bronheim, L. A.; Klingner, A.; Nair, N. P. V.; Galvan, L.; Vergara, L.; Zoch, C. Dept. of Psychiatry, McGill University, Montreal, P.Q., Canada **Differential effects of trazodone in depressed, schizophrenic and geriatric patients.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):23-27, 1974.

A series of systematic studies with trazodone, a newly synthesized pharmaceutical agent, with possible psychoactive properties was designed. Preliminary analysis of the partial results, based on the first three completed clinical trials with depressed, schizophrenic, and geriatric patients, excludes schizophrenia in general as a possible therapeutic indication and provides sufficient data to support the hypothesis that trazodone may be a therapeutically effective agent in the treatment of depressed and/or organic brain syndrome patients. 8 references. (Journal abstract modified)

191190 Brambilla, F.; Guerrini, A.; Riggi, F.; Ricciardi, F. Ospedale Paolo Pini, Via Ippocrate 45, Milano Afforia, Italy **Psychoendocrine investigation in schizophrenia: relationship between pituitary-gonadal function and behavior.** Diseases of the Nervous System. 35(8):362-367, 1974.

Possible connections between the schizophrenic syndrome and the hypothalamo - pituitary - gonadal system are examined. It is assumed that hormonal impairment might correlate with the appearance and development of peculiar behavioral features. The hormonal status and the behavioral parameters were examined before, during and after psychopharmacological therapy and a combination of a psychopharmacological and hormonal treatment in 12 male hebephrenic schizophrenics, aged 18 to 36 years, who were treated with haloperidol and then with haloperidol in combination with chorionic gonadotrophin (HCG). The results obtained revealed a stimulatory effect of the haloperidol plus HCG therapy on the deficient hormonal status. It was evident that a constant correlation existed existed between chemical improvement and behavioral improvement, especially in regard to affective disorders, adjustment to reality, and active behavior. 21 references. (Author abstract modified)

191400 Spring, Carl; Greenberg, Lawrence; Scott, Jimmy; Hopwood, John. Department of Education, University of

California, Davis, CA 95616 **Electrodermal activity in hyperactive boys who are methylphenidate responders.** Psychophysiology. 11(4):436-442, 1974.

The electrodermal activity of hyperactive boys being treated with methylphenidate medication was examined. In one of the hyperactive groups methylphenidate was withheld for approximately 72 hrs before testing. Boys in the other hyperactive group continued to take their usual daily doses of methylphenidate. Normal boys formed a third group. Normal and off drug hyperactive groups differed significantly on specific response amplitude, and trials to habituation. Frequency of nonspecific responses approached significance. These differences indicated lower reactivity in the off drug hyperactive group. Off drug and on drug hyperactive group differed significantly on frequency of nonspecific responses. Trials to habituation approached significance. These differences again indicated lower reactivity in the off drug hyperactive group. 9 references. (Author abstract modified)

191776 Lasting, P. G. Leningrad Scientific Research Psychoneurological Institute imeni V. M. Bekhterev, Leningrad **/The effect of chlorpromazine and amital sodium on the conformity of adolescents under psychiatric observation./** Vliyaniye aminazina i amital-natriya na konformnost' podrostkov, obsleduyemykh v psikhiatricheskoy bol'nitse. In: Saarma, Yu., Voprosy klinischeskoy nevrologii i psikhiatrii. Tartu, U.S.S.R., Tartu University, 1972. 175 p. (p. 12-18). Vol. 9.

The effects of amital sodium and chlorpromazine on the behavior of adolescents under psychiatric observation were investigated. A total of 60 subjects with varied psychopathological disorders were administered a characterologic questionnaire before and after injection. Amital sodium was administered intravenously and chlorpromazine intramuscularly. Examination showed little effect of the drugs on the adolescents' behavior. 8 references. (Author abstract modified)

191828 Weissman, Myrna M.; Klerman, Gerald L.; Paykel, Eugene S.; Prusoff, Brigitte; Hanson, Barbara. Yale Univ. School of Medicine, Dept. of Psychiatry, Depression Research Unit, 100 Park St., New Haven, CT 06511 **Treatment effects on the social adjustment of depressed patients.** Archives of General Psychiatry. 30(6):771-778, 1974.

The effects of maintenance treatment on social adjustment are examined in depressed outpatients randomly assigned to 8 months of amitriptyline hydrochloride, a placebo, or no pill, with or without psychotherapy, using a 2 x 3 factorial design. Results for the 106 patients completing the trial show a significant main effect for psychotherapy apparent only after 6-8 months' treatment. Psychotherapy improved overall adjustment, work performance and communication, and reduced friction and anxious rumination. There was no effect on the patients' social adjustment for amitriptyline and there were no drug/psychotherapy interactions. Results support the value of weekly maintenance psychotherapy in recovering depressives. Evidence for combined treatments exists, since amitriptyline was shown to reduce relapse and prevent symptom return and psychotherapy was shown to enhance adjustment. 37 references. (Author abstract modified)

191830 Rapoport, Judith L.; Quinn, Patricia O.; Bradbard, Gail; Riddle, K. Duane; Brooks, Elizabeth. Dept. of Pediatrics, Georgetown Univ. Hospital, 3800 Reservoir Rd., N.W., Washington, DC 20007 **Imipramine and methylphenidate treatments of hyperactive boys.** Archives of General Psychiatry. 30(6):789-793, 1974.

A double-blind outpatient study is reported comparing imipramine hydrochloride, methylphenidate hydrochloride, and placebo treatments of 76 hyperactive grade school boys. In addition, the predrug behavioral evaluation is examined in detail to provide guidelines for clinics examining these children. Baseline clinic evaluations showed the usefulness of the psychologist's global estimates of attention and behavior disorder, as these ratings predicted teacher rating of classroom behavior better than did psychiatric playroom observations. Parent 4 day diaries of activity and family interaction also predicted teacher ratings, and reflected response to stimulant medication. Although the global judgments of psychiatrists, psychologist, and the pediatrician indicated the superiority of both drugs to a placebo, all measures favored the stimulant drug. The significance of these findings may be limited, however, by the dose of imipramine hydrochloride (80mg) that was lower than in use elsewhere. 21 references. (Author abstract)

191907 Aceto, M. D. Department of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **Effects of CNS agents on nicotine extensor convulsions and lethality in mice and their sedative-antianxiety effects in man.** Pharmacologist. 16(2):205, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the effects of central nervous system agents on nicotine convulsions and lethality in mice and their sedative antianxiety effects in man were reported. Mice were given a CNS agent po and 2 hrs later challenged with an iv LD95 of nicotine. Iproniazid, and tranylcypromine were inactive whereas imipramine, doxepin and amitriptyline were active. For the antianxiety agents, meprobamate was active followed by chlordiazepoxide, and diazepam. The ED50s for drugs designated antipsychotic were: trifluoroperazine 19.0; haloperidol 10.0; thioridazine; and chlorpromazine. Of the antihistamines tested, tripelennamine was the weakest, 40% at 64, followed by promethazine, chlorpheniramine and diphenhydramine. Atropine, benztropine, morphine, meperidine, and alpha-methyl-dl-tyrosine were inactive. There appears to be a good relationship between blockade of nicotine induced extensor convulsions and lethality in mice and sedative antianxiety effects in man. This relationship is especially good for the classes designated antidepressant, antianxiety, and antipsychotic. (Author abstract modified)

191943 Gogerty, J. H.; Eden, P. L.; Fisher, B. A. Sandoz Pharmaceuticals, East Hanover, NJ 07936 **A predictable laboratory model for sedative/hypnotic activity in man.** Pharmacologist. 16(2):238, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a predictable model for sedative/hypnotic activity in man was presented. Fifteen sedative/hypnotic compounds (e.g.,carbamates, ureides, barbiturates, glutarimide derivatives, quinazolones, benzodiazepines and phenothiazines) have been tested in young adult male Cebus apella monkeys. The results indicate excellent correlation between sleep-inducing doses in monkeys and the clinical sedative/hypnotic doses. Effects of the drugs on stage rapid eye movement in monkeys also appear to be predictive of the results observed in humans. In an attempt to predict hangover, sleep and performance were combined using an arduous timing schedule (DRL-1') starting 9 hours post administration of test substances. Results indicate that flurazepam significantly disrupts performance while methaqualone has no effect at threshold sleep inducing doses. (Author abstract modified)

191989 Dalton, W. S.; Martz, R.; Rodda, B. E.; Lemberger, L.; Forney, R. B. Department of Toxicology, Indiana University Medical Center, Indianapolis, IN 46202 **Clinical effects of marihuana secobarbital combination.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the clinical effects of marihuana secobarbital combination were reported. Twelve male volunteers were administered placebo (P) or secobarbital (B) (oral) followed 50 minutes later by marihuana (M) prepared to deliver delta-9-tetrahydrocannabinol (THC) by smoking. Mean heartrates for the treatments were 70 beats/min for P, 76 beats/min for B, 93 beats/min for M, 94 beats/min for M-B. Motor performance was evaluated by a pursuit meter using four patterns. Mean counts/100 sec of a representative pattern were 29381 for P, 35477 for B, 34265 for M, and 41425 for M-B. These and other data do not indicate lack of additivity for marihuana effects and secobarbital effects. (Author abstract modified)

191990 Evans, M. A.; Martz, R.; Lemberger, L.; Rodda, B. E.; Forney, R. B. Department of Toxicology, Indiana University Medical Center, Indianapolis, IN 46202 **Clinical effects of marihuana dextroamphetamine combination.** Pharmacologist. 16(2):281, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, the clinical effects of marihuana dextroamphetamine combination was reported. Six subjects were orally administered either placebo or d-amphetamine (A) followed 1 1/2 hrs later by smoking marihuana (M) prepared to deliver delta-9-tetrahydrocannabinol (THC). Statistical analysis suggested that heartrate and blood pressure increased in an additive manner when both agents were given. Psychomotor performance was evaluated in eleven subjects using A and M prepared to deliver THC. A significant decrease in stability, as reflected by the wobble board, and a significant impairment in motor performance as evaluated by the pursuit meter were produced by both M and M-A combination. No difference could be distinguished between these two treatments. Subjective evaluation, as measured by the modified Cornell Medical Index, demonstrated only additive effects for the combination. (Author abstract modified)

192190 Greenblatt, David J.; Miller, Russell R. Massachusetts General Hospital, Boston, MA 02114 **Rational use of psychotropic drugs: I. hypnotics.** Journal of the Maine Medical Association. 65(8):192-197, 1974.

The use of hypnotics in treating insomnia is reviewed, noting the therapeutic indications for hypnotics and the drugs of choice. A study of the pharmacologic properties of commonly used prescription hypnotic drugs suggests that they do not differ significantly in short-term efficacy nor in the frequency with which they produce hangover. Generically prescribed barbiturates are inexpensive but this is usually outweighed by their numerous hazards and disadvantages. Glutethimide is at least as hazardous as barbiturates and much more expensive. Methaqualone, methyprylon, and ethchlorovynol have no particular advantages. It is thus concluded that flurazepam should be the hypnotic of choice in most clinical circumstances, as it has the fewest disadvantages of the hypnotics. Generically prescribed chloral hydrate can be substituted, if the patient is not taking a coumarin anticoagulant and if drug cost is of major importance. 48 references.

192429 Huber, H. P.; Ehlers, W. Psychological Department, University of Dusseldorf, Dusseldorf, Germany **The effects of Hoe 36 801 on muscle activity and blood pressure, on attention and concentration, on time judgement and subjective responses in neurotics and normals.** Activitas Nervosa Superior (Praha). 16(1):71-73, 1974.

Changes in activation due to Hoe 36 801 on different levels of integration were studied with a variety of indicators. The diastolic blood pressure was found to change significantly under the influence of Hoe 36 801. Neurotics and normals were shown to be differentiated in the d-2 test performance. The data revealed a significant influence of the drug on time estimation. There were no significant drug effects on subjective responses. 11 references.

192871 Curry, Stephen H. Dept. of Pharmacology and Therapeutics, London Hospital Medical College, University of London, London, England **Concentration-effect relationships with major and minor tranquilizers.** Clinical Pharmacology and Therapeutics. 16(1,Part 2):192-197, 1974.

At the Second Deer Lodge Conference on Clinical Pharmacology, held in June 1973 in Hershey, Pennsylvania concentration - effect relationships with major and minor tranquilizers were reported. Relationships between the effects of centrally acting drugs and concentrations of the pharmacologically active molecules in plasma can take a wide variety of forms, ranging from simple direct relationships, for instance those involving effects on reaction time, to extremely complex relationships, such as those involving clinical rating of psychopathology. A number of forms of relationships have been revealed with glutethimide, nordiazepam, and chlorpromazine, and a brief review was presented of the current status of studies of the relationship between concentration and effect for these compounds. 15 references. (Author abstract)

15 TOXICOLOGY AND SIDE EFFECTS

187644 Naylor, G. J.; Dick, D. A. T.; Dick, E. G.; Moody, J. P. Department of Psychiatry, University of Dundee, Dundee DD1 4HN, United Kingdom **Lithium therapy and erythrocyte membrane cation carrier.** Psychopharmacologia (Berlin). 37(1):81-86, 1974.

Changes induced by lithium treatment in the erythrocyte membrane cation carrier were investigated. Plasma cortisol and erythrocyte Na-K ATPase, ouabain sensitive K+ influx, lithium, sodium and potassium concentrations were measured twice when patients were on placebo and twice when they were on lithium therapy. The erythrocyte Na-K ATPase was significantly higher during the lithium than during the placebo treatment period, whereas the other biochemical values measured showed no significant difference between the two phases. 18 references. (Author abstract).

187786 O'Connell, Ralph A. 144 West 12th St., New York, NY 10011 **Lithium carbonate: psychiatric indications and medical complications.** New York State Journal of Medicine. 74(4):649-653, 1974.

Psychiatric indications for the medical complications of lithium carbonate in control of manic episodes in manic-depressive psychosis are reviewed. A 5 year experience with over 75 patients on lithium carbonate and pertinent reports from world literature on the topic are presented. Lithium carbonate is suggested for the treatment and prevention of manic-depressive psychoses. Acute toxic reactions and long-term complications are described. Therapeutic advantages of lithium carbonate are

evaluated against the possible complications. Precautions necessary in the application of lithium carbonate for aged and pregnant patients are noted. 39 references. (Author abstract)

187787 Levy, Walter; Wisniewski, Krystyna. 12 East 88th St., New York, NY 10028 **Chlorpromazine causing extrapyramidal dysfunction in newborn infant of psychotic mother.** New York State Journal of Medicine. 74(4):684-685, 1974.

A neonate with Parkinsonism following maternal ingestion of chlorpromazine (Thorazine) as part of psychosis therapy is studied. Research shows that the extrapyramidal symptoms persisted for nearly 6 months. Diphenhydramine hydrochloride (Benadryl) was administered for 6 months before the symptoms subsided. The pharmacologic action of thorazine and benadryl on the central nervous system is reviewed. Results suggest that caution should be exerted in dispensing the phenothiazine drugs to pregnant women, since toxicity in the infant with persistent extrapyramidal symptoms may ensue. 19 references. (Author abstract)

187837 Chessen, Douglas H.; Geha, Dwight G.; Salzman, Carl. Dept. of Psychiatry, Harvard Medical School, Boston, MA **ECT, glaucoma, and prolonged apnea.** Diseases of the Nervous System. 35(4):152-153, 1974.

The development of prolonged apnea in the middle of an electroconvulsive therapy (ECT) series given to a depressed elderly woman is reported. A reaction to a change in the patient's eyedrops from pilocarpine-epinephrine to echothiophate was noted as the cause of apnea. The necessity for careful medical screening of all patients for concurrent medical treatment is expressed. The importance of noting any introduction or changes in medication, even if they occurred 2 months earlier is underscored. The potential hazard of echothiophate - succinylcholine interaction is stressed. It is suggested that patients should not be given succinylcholine for a minimum of 3 weeks after echothiophate has been discontinued. 9 references.

188094 Reimer, Donald R.; Mohan, Jagan; Nagaswami, Subramoney. Dept. of Neurology, Topeka VA Hospital, Topeka, KS 66622 **Heat dyscontrol syndrome in patients receiving antipsychotic, antidepressant and antiparkinson drug therapy.** Journal of the Florida Medical Association. 61(7):573-574, 1974.

A relatively new etiological type of iatrogenic, hyperpyretic crisis is presented and the pathophysiology of this syndrome is discussed. A depressed patient who was taking a tricyclic antidepressant, an aliphatic phenothiazine, and also an antiparkinson type drug is described. In addition to the drug therapy, the patient was allowed uncontrolled exposure to midsummer heat that precipitated a hyperpyretic crisis in this relatively poikilothermic patient. The treatment of this type of patient is presented to show that death is an imminent feature of this iatrogenic phenomena. It is hoped that treating physicians will avoid this type of polypharmacy. 11 references. (Journal abstract modified)

188114 Snyder, Solomon; Greenberg, David; Yamamura, Henry I. Johns Hopkins University School of Medicine, Dept. of Pharmacology and Experimental Therapeutics, 725 N. Wolfe St., Baltimore, MD 21205 **Antischizophrenic drugs and brain cholinergic receptors: affinity for muscarinic sites predicts extrapyramidal effects.** Archives of General Psychiatry. 31(1):58-61, 1974.

The influence of a variety of phenothiazines and butyrophenones on the brain's receptor for the muscarinic action of acetylcholine was studied. Extrapyramidal effects are inversely proportional to affinity for the muscarinic receptor. Thus, drugs such as clozapine and thioridazine hydrochloride apparently owe their low incidence of extrapyramidal effects to anticholinergic properties that compensate for their intrinsic extrapyramidal effects. These findings provide a means to predict extrapyramidal actions of new potential antischizophrenic drugs. 26 references. (Author abstract modified)

188312 Ayd, Frank J., Jr. Department of Professional Education and Research, Taylor Manor Hospital, Ellicott City, MD **Side effects of depot fluphenazines.** Comprehensive Psychiatry. 15(4):277-284, 1974.

Data on the safety of the injectable forms of fluphenazine, fluphenazine enanthate and fluphenazine decanoate, is given by a review of the side-effects that have occurred in over 300,000 patients treated with these drugs in the past 9 years. Clinical experience has shown that serious adverse reactions to depot fluphenazines are no more frequent, and usually less so, than similar reactions to other potent oral neuroleptics. Clinicians have no more reason to be concerned about the possible consequences of injecting a depot neuroleptic than they have to be concerned about the consequences of administering oral neuroleptics. 25 references.

188414 Lieberman, Abraham N.; Shupack, Jerome L. New York University School of Medicine, 566 First Ave., New York, NY 10016 **Levodopa and melanoma.** Neurology. 24(4):340-343, 1974.

Three case histories of patients with known melanomas undergoing levodopa treatment are reported. Levodopa was administered to these subjects with Parkinson's disease and known neoplasms or pigmented lesions. Levodopa was discontinued in the first man, who had a benign pigmented nevue for 20 years. The second man died. The third patient remains well 2 years later. In two additional cases in the literature, a temporal association was found between initiation of levodopa and growth of melanoma. It is concluded that levodopa might influence melanoma in two ways: direct incorporation into the tumor or indirectly through growth hormone. It is suggested that patients receiving the drug be observed for changes in pigmented lesions. 19 references. (Journal abstract modified)

188450 Miyashita, Shunichi; Ogura, Masami; Harada, Kenichi. Department of Neuropsychiatry, Shinshu University School of Medicine, Japan **The problems of the clinical usage of nitrazepam: suppressive effects on the pharyngeal reflex and the coma, using other tranquilizers at the same time.** Clinical Psychiatry (Tokyo). 15(8):875-879, 1973.

The suppressive effects of nitrazepam (Ni) on the pharyngeal reflex are discussed, as well as coma induced by the combination of Ni and other tranquilizers. Two case studies of attempted suicides, using Ni with other tranquilizers, are provided; both resuled in comas. The case of a man treated with Ni and minor tranquilizers is described. He showed somnolent tendency after each treatment, and after the fourth treatment disturbance of the pharyngeal reflex developed and he choked to death on a piece of food. The final case described concerns an epileptic woman treated with Ni. After two treatments, she complained of difficulty in swallowing. Immediately after termination of Ni treatment, the symptom disappeared. 11 references.

188886 no author. no address **Mental changes in Parkinsonism.** British Medical Journal (London). No. 5909:1-2, 1974.

The question of whether mental changes in Parkinsonism are the result of neurological deficit or are caused by treatment with levodopa is examined. It is noted that it is not possible to draw any firm conclusions when many thousands of Parkinsonian patients have now been receiving substantial doses of levodopa for several years and the reports of irreversible mental deterioration are limited. However, accounts of stupor and dementia should alert physicians to continue careful surveillance of all patients on long-term therapy with levodopa. It is only by notification of all unexpected findings to the Committee on Safety of Medicines that sufficient experience can be built up for a causal relationship to be established or refuted. 13 references.

189042 Baloch, N. Severalls Hospital, Colchester, Essex, England **'Steroid psychosis': a case report.** British Journal of Psychiatry (London). 124:545-546, 1974.

The case of a 41-year-old who suffered from mood alterations, an organic confusional state and electroencephalographic (EEG) changes after administration of a small dose of prednisolone for an arthritic condition is reported. After 72 hours, symptoms subsided and the patient was advised to have alternative therapy for rheumatoid arthritis. 4 references.

189099 West, A. Preston. 5050 South Lake Shore Drive, Chicago, IL 60615 **Interaction of low-dose amphetamine use with schizophrenia in outpatients: three case reports.** American Journal of Psychiatry. 131(3):321-323, 1974.

An exacerbation of acute schizophrenia by amphetamine was demonstrated. The case histories presented suggest that the dosage of amphetamine often prescribed for dieting may precipitate psychotic symptoms in outpatient schizophrenics who are not known to be clinically ill when the drugs are prescribed. 6 references. (Author abstract modified)

189173 Encinoza, Oscar. Dept. of Neurology, School of Medicine, University of Los Andes, Merida, Venezuela **Nerve conduction velocity in patients on long-term diphenylhydantoin therapy.** Epilepsia (Amsterdam). 15(2):147-154, 1974.

Motor conduction velocities along the median, ulnar, peroneal, and posterior tibial nerves and distal sensory latency of the median nerve were determined in 300 patients on diphenylhydantoin therapy who did not present clinical evidence of either peripheral neuropathy or toxicity. Slowed conduction was found in 156 patients (52%). Most frequent were prolonged sensory latency of the median nerve (44%) and motor conduction in the legs (33%). Abnormal findings were more frequent in patients over 20 years of age, when the dose was 4.5mg/kg or more and the duration of medication 4 years or more. 8 references. (Author abstract)

189512 Saraf, Kishore R.; Klein, Donald F.; Gittelman-Klein, Rachel; Groff, Stephen. Hillside Hospital, 75-59 263 Street, Glen Oaks, NY 11004 **Imipramine side effects in children.** Psychopharmacologia (Berlin). 37(3):265-274, 1974.

The incidence, range and severity of side-effects in 65 children and young adolescents receiving imipramine treatment are compared with those occurring in 37 children and young adolescents receiving placebo. Minor side-effects occurred in 83% of the imipramine group and in 70% of the placebo group. Just under 5% of the children in the imipramine group and in 70% of the placebo group. Just under 5% of the children in the imipramine group had significant side-effects but none were serious enough to necessitate drug withdrawal. The majority of side-effects in both groups occurred during the first weeks of treatment. There may be serious individual idiosyncrasies to high dosage of imipramine, as possibly suggested by the sudden death of one 6-year-old girl during imipramine treatment. 30 references. (Author abstract)

189606 Joubert, P. H.; Olivier, J. A. Department of Pharmacology, University of Orange Free State Medical School, Bloemfontein, South Africa **Fatal suicidal ingestion of thioridazine.** Clinical Toxicology. 7(2):133-138, 1974.

A case of apparent recovery from the acute effects of suicidal thioridazine ingestion and unexpected death two days later is presented. A 27-year-old male was admitted to hospital in coma after ingesting 3gm of thioridazine. His family found him unconscious in bed early in the morning and the exact time of ingestion was unknown. Endotracheal intubation was performed and copious amounts of blood stained forthy fluid aspirated from both lungs. The patient's pulmonary signs improved considerably after tracheostomy and bronchial lavage, but crepitations and rhonchi persisted at the right lung base. The patient's general condition continued improving and on the third day the tracheostomy tube was removed. At about 3 a.m. the next morning he suddenly became dyspnoeic with recurrence of pulmonary edema and despite resuscitative measures developed a cardiac standstill and died. Microscopic examination of various organs showed nonspecific congestion. Gross abnormalities were limited to the lungs and kidneys. Extensive congestion, intraalveolar edema, and hemorrhage were present in both lungs. 7 references.

189902 Helling, Dennis K.; Strong, Kirk H. University of Iowa College of Pharmacy, Iowa City, IA 52242 **Methaqualone: an irrational hypnotic.** Journal of the Iowa Medical Society. 64(8):351-354, 1974.

Concern is expressed regarding the use of methaqualone; it is noted as the third most commonly prescribed nonbarbiturate hypnotic in the country. Methaqualone appears to be an effective sedative hypnotic but has not demonstrated any advantage over other sedative hypnotics. It is being widely abused, possesses a narrow therapeutic range and may produce serious toxic reactions, has a potential for both physical and psychological dependence, and therefore cannot be considered a drug desirable to medical practice. (Author abstract modified)

190258 Azarnoff, Daniel L. Department of Medicine and Pharmacology, University of Kansas Medical Center, Kansas City, KS **Drug interactions.** Israel Journal of Medical Sciences (Jerusalem). 10(4):346-348, 1974.

Important factors arising from the concomitant administration of various drugs are discussed. Alteration of pH by antacids, competition for binding sites by two or more drugs, metabolic rate as the determinant of drug effect, and the addictive affect of alcohol with other central nervous system depressants are evaluated. 8 references.

191035 Jacobson, Gary; Baldessarini, Ross J.; Manschreck, Theo. Dept. of Psychiatry, Massachusetts General Hospital, Boston, MA 02114 **Tardive and withdrawal dyskinesia associated with haloperidol.** American Journal of Psychiatry. 131(8):910-912, 1974.

Four cases of tardive and withdrawal dynskinesia attributable to treatment with 4-20mg of haloperidol daily for more than a year are reported. Two cases involved temporary oral - facial dyskinesias and the others a more persistent complex mixture of neurological features. The possibility that tardive

dyskinesia may be associated with the butyrophenones in addition to other antipsychotic agents should be considered. 29 references. (Journal abstract modified)

191142 Villeneuve, A.; Gautier, J.; Jus, A.; Perron, D. Hopital St.-Michel-Archange, Quebec, P.Q., Canada **The effect of lithium on thyroid in man.** Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):75-80, 1974.

Thyroid changes were studied in a population of 149 patients treated with lithium for periods of time varying from 16 to 152 weeks. It was found that hypothyroidism occurred in 22 patients of whom two were male and 20 were female. It is concluded that the risk of hypothyroidism during lithium therapy appears higher than in the general population and greater in females than in males. It is noted that age, length of treatment or type of psychosis did not seem to influence the risk of thyroid disturbances. 12 references. (Author abstract modified)

191187 Spring, Gottfried K. Dept. of Psychiatry, Case Western Reserve Univ., Cleveland, OH 44106 **Hazards of lithium prophylaxis.** Diseases of the Nervous System. 35(8):351-354, 1974.

The potential hazards of prophylactic lithium and the problems of its indiscriminate use are illustrated in depth by two cases of severe intoxication with prophylactic lithium, one of which nearly ended fatally. Symptoms, mechanisms and successful medical management of lithium toxicity are also described. The need for all physicians and psychiatrists to be familiar with lithium carbonate and the potential hazards of its use is stressed. The cases discussed demonstrate the need for the psychiatrist to be part of the medical team, in order to assure proper patient care. 16 references. (Author abstract modified)

191188 Milstein, Victor; Small, Joyce G. Larue D. Carter Memorial Hospital, 1315 West 10th St., Indianapolis, IN 46202 **Photic responses in 'minimal brain dysfunction'.** Diseases of the Nervous System. 35(8):355-357, 1974.

The electroencephalographic influences of a long acting nonamphetamine stimulant drug, magnesium pemoline, were examined in minimal brain damaged children. Ss were 20 children aged 6 to 12. Findings supported the position that drugs effective in the treatment of childhood hyperkinesis exerted a stimulant effect upon the central nervous system (CNS). Evidence from the use of a long-acting chemical without reported biphasic or paradoxical pharmacologic influence does not suggest that the CNS effects were atypical in such children. It is considered that some of the controversy in the literature might be related to the short time course of action and possible biphasic effects of other drugs, although further studies are suggested. The mechanisms by which drugs that stimulate the CNS on the neurophysiological level can be associated with reduced excitement and inhibition of behavior remains an important topic for investigation. 17 references.

191215 Robertson, James F. Willsmere Hospital, Kew, Victoria 3101, Australia **Mental illness or metal illness? Bismuth subgallate.** Medical Journal of Australia (Sidney). 1(22):887-888, 1974.

Neuropsychiatric symptoms associated with bismuth subgallate ingestion in four of nine colostomy patients are described. Acute - on - chronic - brain syndrome occurred in one patient admitted to a psychogeriatric hospital. 5 references. (Author abstract)

191959 El-Yousef, M. Khaled; Mahler, D. Hal. Vanderbilt University, Nashville, TN 37203 **The effect of conjugated estrogens on plasma butaperazine levels in women.** Pharmacologist. 16(2):256, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a randomly assigned control experimental grouping with a crossover design was utilized to study the effects of conjugated estrogens on plasma levels of butaperazine attained with set oral doses of the drug. Twenty female subjects who had normal blood chemistry and liver function tests had both a single dose with 24 hour sequential blood collection and maintenance studies. All the postmenopausal women studied showed significantly increased AUC and mean of maintenance levels while they received conjugated estrogens as to placebo. There was essentially no change in either measure with estrogens in either the ovulatory or the premenopausal subjects studied. (Author abstract modified)

191982 Yen-Koo, H. C.; Balazs, T.; Davis, D. A. Division of Drug Biology, CPRT, Bureau of Drugs, FDA, Washington, DC **A method for testing drug induced Parkinsonian-like effect.** Pharmacologist. 16(2):264, 1974.

At the fall meeting of the American Society for Pharmacology and Experimental Therapeutics, a method for testing drug induced Parkinsonian like effect is described. Parkinsonian syndrome (PS) inducing drugs inhibited the DOPA induced biting behavior. The criterion for effectiveness was the prevention of the biting or gnawing behavior. Prevention indexes (PI) were calculated from LD50/ED50. Thioridazine and chlordiazepoxide, dopa, apomorphine, amphetamine and thozalinone showed the least inhibition against the agents and PIs were 4.3, 1.5, 1.9and 35.3, and 17.7, 15.3, 18.4and 9.2, respectively. PIs for haloperidol, chlorpromazine and perphenazine were higher and comparable. Trifluoperazine produced highest PIs against the four agents. (Author abstract modified)

192084 Jarvik, Lissy F.; Yen, Fu-Sun; Dahlberg, Charles C.; Fleiss, Joseph L.; Jaffe, Joseph; Kato, Takashi; Moralishvili, Emelia. Department of Psychiatry, Center for Health Sciences, UCLA, Los Angeles, CA **Chromosome examinations after medically administered lysergic acid diethylamide and dextroamphetamine.** Diseases of the Nervous System. 35(9):399-407, 1974.

The chromosomes in peripheral leukocytes of persons given lysergic acid diethylamide (LSD) and dextroamphetamine (DA) under medical supervision, following a double-blind design, were monitored and in vitro experiments with LSD on cultures derived from the same subjects were performed to determine individual differences in chromosomal breakage resulting from the addition of the drugs. The results demonstrate again that on the average, the addition of LSD in vitro leads to chromosome damage in excess of that observed in cultures without such added LSD, even though nearly all of the in vitro experiments were carried out on blood cultures derived from patients already started on the drug regime in vivo. By contrast, present data provides no evidence for a measurable detrimental effect of LSD and DA when administered under medical supervision. 36 references. (Author abstract modified)

192513 Johnson, D. A. W. Crumpsall Hospital, Manchester, England **Psychiatric symptoms produced by drugs.** Nursing Mirror and Midwives Journal (London). 138(14):72-73, 1974.

It is recommended that evaluation of any patient psychiatrically or emotionally disturbed include a full physical examination and a careful consideration of all drugs and medications that may have been taken. Clinical syndromes caused by drug reactions can be so varied that drug or dosage changes may have a temporal relationship with a change in mental state. Features of the effects of diuretics, antibiotics, analgesics and antipyretics, hypnotics, anticonvulsants, steroid hormones, stimulants, antihistamines, drugs acting on the cardiovascular and respiratory systems, and psychiatric drugs are emphasized.

16 METHODS DEVELOPMENT

187639 Hansen, Christian Eggert; Larsen, Niels-Erik. Dept. O, State Mental Hospital, DK-2600 Glostrup, Denmark **Perphenazine concentrations in human whole blood: a pilot study during anti-psychotic therapy using different administration forms.** Psychopharmacologia (Berlin). 37(1):31-36, 1974.

The elimination rate of Perphenazine (PPZ) from human blood during antipsychotic therapy involving various administration forms was measured. A new specific and highly sensitive gas chromatographic method showed concentrations of 0.2microgram PPZ/1 whole blood could be assayed with a sufficient degree of accuracy. In acutely psychotic patients the PPZ levels were studied after administration in three different ways: A) as single doses of PPZ given intramuscularly, B) as multiple doses of PPZ given orally, and C) as single doses of PPZ enanthate given intramuscularly. The highest PPZ concentration, 7.4microgram/1, was measured in experiment C. Neurological side-effects were registered, and their relation to blood concentrations of PPZ are briefly discussed. 13 references. (Author abstract).

191603 Seevers, M. H. Department of Pharmacology, University of Michigan, Ann Arbor, MI **Methodology for the evaluation of pentazocine, prototype of the new morphine agonist-antagonist analgesics.** Intern. J. of Clinical Pharmacology, Therapy, and Toxicology (Munchen). 9(3):167-173, 1974.

Methodology is described for the laboratory and clinical evaluation of pain relief and the dependence liability of pentazocine, a prototype of the new morphine agonist - antagonist analgesics. The laboratory and clinical evaluation of these new analgesics requires special techniques to determine the relative strength of the two opposing components. Such knowledge is essential to the accurate assay of pain relief and to the determination of the physical dependence capacity of this unique class of analgesics vis-a-vis morphine. These techniques are described and the results shown to be valid and confirmed by extensive worldwide clinical use. 9 references. (Author abstract modified)

17 MISCELLANEOUS

187488 Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **In appreciation of basic biochemical research in mental health. (Unpublished paper).** Bethesda, NIMH, 1974. 13 p.

The contributions of basic physiological, biochemical and pharmacological studies to the mental health of man were discussed at a conference on 'Critical Issues Related to Mental Health Research', sponsored by the National Association for Mental Health and held in Reston, Virginia in February, 1974. Basic research findings of the past 20 years are summarized in terms of relevance to the brain and thus to applied psychiatry. The importance of understanding central nervous system functions is described in terms of psychotropic drug development.

187840 Sheppard, Charles; Beyel, Virginia; Fracchia, John; Merlis, Sidney. Central Islip State Hospital, New York, NY **Polypharmacy in psychiatry: a multi-state comparison of psychotropic drug combinations.** Diseases of the Nervous System. 35(4):183-189, 1974.

Data derived from a sample of psychiatrists from four states having large patient and psychiatric populations is examined. A single case questionnaire survey is used to identify the types of drugs used in combination. Results show that the sampled psychiatrists use a broad array of drug combinations. Chlorpromazine - trifluoperazine is the combination showing most frequent use. An analysis of combinations by geographic area is presented. It is suggested that the proliferation of potent but partially effective psychotropic drugs has advanced the development of unnecessary treatment procedures. Areas of research into the topic of drug combinations are noted. 7 references.

187959 Thiele, Wolfgang. D-7102 Weinsberg, Germany **/Pain and psychopharmaceuticals./** Schmerz und Psychopharmaka. Schweizer Archiv fur Neurologie, Neurochirurgie und Psychiatrie (Zurich). 112(1):143-154, 1973.

Application of pharmaceutical agents, particularly neuroleptics, in treating pain is discussed. Many have noticed that two types of pain exist: one caused by biological affectation of the nerves transmitted to the cerebral spinal system; the other is a thalamic activity -- a sensation of feeling pain by an unbiological phenomenon. Standard morphines and combinations of analgesics and phenothiazines have a limited effect, unfavorable side-effects, and can be toxic. Phenothiazines and muscle relaxing tranquilizers have shown positive results in certain ailments of the second category. A long list of neuroleptics is given including their use and their positive effects. 150 references.

188149 Goldberg, Ivan K.; Malitz, Sidney; Kutscher, Austin H. no address **Psychopharmacological agents for the terminally ill and bereaved.** New York, Columbia University, 1973. 339 p. $12.50.

Multidisciplinary selections relevant to psychopharmacological treatment of the dying and grieving are presented. Topics considered include: LSD treatment for the terminal patient; use of chlorpromazine; the relation of drug management to patient personality type; the changes in drug need in various phases of the dying process; use of tranquilizers for the bereaved; and the death of children.

188533 Ventura, Marlene Slawson. State University of New York, Buffalo, NY 14214 **A look at restraining practices and the use of psychotropic drugs.** Journal of Psychiatric Nursing and Mental Health Services. 12(3):3-9, 1974.

The use of psychotropic drugs in the treatment of the mentally ill and the changes in administrative policy which have reduced restraining practices are reviewed. It is suggested that drug therapy made the policy changes possible. The introduction of psychotropic drugs coincided with a period of renewed interest in the influence of social settings upon the behavior of patients in mental hospitals and with the development of the therapeutic community concept. A variety of interpretations from England, Scotland, and the U.S. is presented. 18 references.

189074 Stevenson, Ian; Buckman, John; Smith, Burke M.; Hain, Jack D. Department of Psychiatry, Box 152, University of Virginia Medical Center, Charlottesville, VA 22901 **The use of drugs in psychiatric interviews: some interpretations based on controlled experiments.** American Journal of Psychiatry. 131(6):707-710, 1974.

Some interpretations on the use of drugs in psychiatric interviews based on controlled experiments are presented. Patients exhibited less expression of emotion than is usually reported in drug interviews. This remained true even when freer conditions were instituted. The general research ambiance may have inhibited patients and perhaps interviewers. Many patients reported improvement in feelings and symptoms; these improvements showed no correlation with the expression during the interview of negative affects or with depression. Desuppression did correlate with indications of improvement. Drugs may provide a chemical buffer against negative feelings and thus enable the patient to talk about stressful experiences and integrate them with his current situation. 25 references. (Author abstract modified)

189297 Audio-Visual Services, Lewis Hall, University of Washington, Seattle, WA 98195 (206-543-2500) U-W (R)$7 **Drug Therapies in Crisis Management.** One half inch videotape (sony) B&W 47 min, 1972.

Drug therapies in crisis management are explored by Dr. Lawrence Halpern, Department of Pharmacology, and Dr. Perry Marshall, Department of Psychiatry, of the University of Washington.

189331 Udabe, Ronaldo Ucha. Rivadavia 1823 80B, Buenos Aires, Argentina **Biochemistry and psychiatry with special reference to psychopharmacology.** Psychotherapy and Psychosomatics (Basel). 23(1-6):179-187, 1974.

At the second Congress of the International College of Psychosomatic Medicine in Amsterdam in 1973, three discoveries concerning biochemical considerations in normal behavior and the causes of mental illness were presented: the role of prostoglandins in controlling release and uptake of neurotransmitters; the role of cyclic adenosine monophosphate and its synthesizing enzyme, adenyl cyclase, in neural transmission; and the role of certain neurohormones within the central nervous system. It was felt that these discoveries reflect key components in the relationship between biochemistry and psychiatry. A discussion by E. Cuenca raises more questions in the areas of psychotherapeutics, pharmacokinetics, and pharmacogenetics. 14 references. (Author abstract modified)

189610 no author. no address **Attack on the gate theory of pain.** Medical World News. 15(26):19-20, 1974.

Highlights of a meeting of the American Neurological Association held in conjunction with the Association of British Neurologists are reported. Consideration was given to: increased understanding of pain which throws doubt on the classic gate control theory; further evidence of the efficacy of L-dopa for parkinsonism; and the effectiveness of amitriptyline for prophylactic treatment of severe migraine headaches associated with depression.

189640 Isenberg, Phillip L.; Mahnke, Mark W.; Shields, Walker E., Jr. Outpatient Clinic, McLean Hospital, Belmont, MA **Medication groups for continuing care.** Hospital & Community Psychiatry. 25(8):517-519, 1974.

An outpatient clinic in a community setting using medication groups to monitor and improve the effectiveness of psychotropic drugs was studied. A third year psychiatric resident leads the groups, assisted by a staff nurse. An intake team selects patients and sets up attendance schedules. During the meeting the resident checks with each patient about his medication and makes any adjustments necessary; the group members then discuss problems in daily living. 1 preference. (Author abstract modified)

189924 Winstead, Daniel K.; Anderson, Arthur; Eilers, M. Kathleen; Blackwell, Barry; Zaremba, A. Lance. Dept. of Psychiatry, College of Medicine, University of Cincinnati, 234 Goodman Street, Cincinnati, OH 45229 **Diazepam on demand: drug-seeking behavior in psychiatric inpatients.** Archives of General Psychiatry. 30(3):349-351, 1974.

In a study of drug seeking behavior, patients admitted to a psychiatric ward were allowed to seek diazepam (Valium) for 6 months on demand. Details of 689 requests by 83 patients were recorded. Drug seeking behavior was expressed as a drug seeking index (DSI) based on the ratio of requests to duration of stay. For the whole ward there was an increasing trend in drug use and nurses' attitudes became more favorable. Over 35% of the patients never sought drugs and requests were made on the average of only once every 3 days. The features correlated with DSI were anxiety, being female, White, and having an elevated psychasthenia scale on the Minnesota Multiphasic Personality Inventory. The DSI was not related to either diagnosis or use of major psychiatric drugs. It is concluded that extensive use of antianxiety drugs might be reduced by prescribing them when necessary rather than on fixed schedules. 9 references. (Journal abstract modified)

190144 Cole, Jonathan O.; Stotsky, Bernard A. Dept. of Psychiatry, Temple Univ. Medical School, Philadelphia, PA **Improving psychiatric drug therapy: a matter of dosage and choice.** Geriatrics. 29(6):74-78, 1974.

Dosage and choice of drugs in psychiatric drug therapy for the aged are discussed. Three guidelines for drug dosage to avoid toxic side-effects and yet to be effective are given. Special problems of patients administered antipsychotic agents are cited. Drugs evaluated include antipsychotics, antianxiety agents and sedative - hypnotics, and antidepressants versus electroconvulsive therapy. It is warned that psychiatric syndromes in the elderly may be caused by drugs; in some cases diagnosis and treatment of a medical condition precipitating psychiatric symptoms is more important than use of psychoactive drugs. 40 references.

190236 Irwin, Samuel. Dept. of Psychaitry, University of Oregon Medical School, Portland, OR **How to prescribe psychoactive drugs.** Bulletin of the Menninger Clinic. 38(1):1-13, 1974.

Guidelines for prescribing psychoactive drugs are discussed. Factors affecting the response to drugs are described as excitement and distress arousal, stimulus detachment or involvement, relaxation, and mode of operant response. Some factors in patient assessment for therapy are degree of behavioral arousal present, under or over - activity, distress, sleep problems, problems of drug dependence, and medical complaints. Direct and indirect drug actions, value of interrupted drug therapy, and drug combination therapy are discussed, and the value of the participatory role of the patient and tolerance development are included.

190237 Irwin, Samuel. Dept. of Psychiatry, University of Oregon Medical School, Portland, OR **The uses and relative hazard potential of psychoactive drugs.** Bulletin of the Menninger Clinic. 38(1):14-48, 1974.

Information on the pharmacology, relative therapeutic efficacy, and hazard potential of psychoactive drugs is presented. Tables are used to examined the percentage of individual - social hazard potential; drugs in order of diminishing hazard; criteria for rating hazard potential; relative hypnotic properties; relative stimulant properties; and profiles of psychoactive drug action. Each major category of drug is examined.

190240 Marsella, Anthony J.; Price-Williams, Douglas. Hawaii Research Program, Social Science Research Institute, University of Hawaii, Honolulu, HI **A note on epistemic organization and hallucinogens.** Bulletin of the Menninger Clinic. 38(1):70-72, 1974.

The conditioning of variant models of time, space, and cause - effect related to hallucinogens was studied. Over long periods of hallucinogen use, a person develops a new and conflicting epistemic organization that extends beyond the actual drug states. It is felt that the new epistemic organizations which develop may begin to infleunce 'normal' life experiences.

190305 McNair, Douglas M. Psychopharmacology Laboratory, Boston University School of Medicine, 700 Harrison Avenue, Boston, MA 02118 **Self-evaluations of antidepressants.** Psychopharmacologia (Berlin). 37(4):281-302, 1974.

Antidepressant clinical drug trials conducted from 1955-1972 are analyzed to determine the most frequently used patient self-rating scales and to estimate their relative sensitivities (validities). Other analyses suggest how the methodology of the trials may have influenced measurement sensitivity. Interpretive problems are discussed, and some tentiative recommendations are presented. 99 references. (Author abstract)

191048 AMA Department of Drugs. no address **AMA drug evaluations.** 2nd ed., Acton, MA, Publishing Sciences Group, 1973. 1031 p. $22.00.

Classes of drugs are described briefly, followed by sections on adverse reactions and precautions. Specific drugs in each class are described and evaluated, with the inclusion of structural formulas.

191139 Galvan, L.; Ucha, R.; Vergara, L.; Zoch, C.; Ban, T. A. Dept. of Psychiatry, McGill University, Montreal, P.Q., Canada **A comparison of clinically used psychoactive drugs in**

four Latin American countries and in Canada (Argentina, Costa Rica, Mexico and Panama). Intern. J. of Clinical Pharmacology, Therapy and Toxicology (Munchen). 9(1):28-31, 1974.

Psychopharmacological practices were compared and found to be essentially the same in four Latin American countries (Argentina, Costa Rica, Mexico, and Panama) and in Canada. Among the anxiolytic sedatives, the use of benzodiazepines and propanediols, and among the thymoleptics, monoamine oxidase inhibitors were found to be less frequently employed than tricyclic antidepressants. It was also found that there are more neuroleptic preparations available in the four Latin American countries than in Canada. 4 references. (Author abstract modified)

191604 Ventafridda, V.; Spreavice, R. Servizio di Terapia del dolore e Riabilitazione, Instituto Nazionale per lo Studie e la Cura dei Tumori, Milano, Italy **Considerations on the use of analgesic drugs in different stages of neoplastic diseases.** Intern. J. of Clinical Pharmacology, Therapy, and Toxicology (Munchen). 9(3):174-179, 1974.

Some criteria of selection of drugs for treatment of pain in cancer patients are presented and discussed. The stage of evolution of the neoplastic process and the severity of the pain are considered as the most important factors to be taken into consideration in this selection, and the use of nonnarcotic analgesics is recommended during the early stages, while narcotic analgesics may be used without restrictions in the terminal stage only. Some results of an analysis of pain charts filled out by the patients are presented, showing that satisfactory pain relief can be obtained in the majority of the cases during the early stages with nonnarcotic analgesics. The combination of analgesics with other drugs, with special reference to psychotropic drugs, is also briefly discussed and is recommended for solution of some therapeutic problems. 5 references. (Author abstract)

191606 Twycross, R. G. St. Christopher's Hospice, S1-53 Lawrie Park Road, London SE26 6DZ, England **Clinical experience with diamorphine in advanced malignant disease.** Intern. J. of Clinical Pharmacology, Therapy, and Toxicology (Munchen). 9(3):184-198, 1974.

Clinical experience with diamorphine in cases of advanced cancer is reviewed, based on data obtained from its use 500 terminal patients treated in a London hospital. It was found that: (1) although most patients received parenteral treatment during the last 12-48 hours due to increasing debility, the majority can be maintained on orally administered diamorphine prior to this time; (2) there is no single optimal dose or maximum effective dose of diamorphine; (3) the prescription of the drug does not by itself lead to impariment of mental faculties; (4) tolerance is not a practical problem; (5) psychological dependence does not occur; (6) physical dependence may develop, but this does not appear to prevent the downward adjustment of the dose when it is considered clinically feasible. 9 references. (Author abstract modified)

191607 Heubel, F. D-355 Marburg/Lahn, Pharmakologisches Institut Lahnberge, Germany **/Nonsedating dosages of diazepam and phenobarbital in the reduction of neonatal bilirubin levels./** Diazepam und Phenobarbital bei der Senkung des Neugeborenen-Bilirubinspiegels durch nichtsedierende Dosen. Intern. J. of Clinical Pharmacology, Therapy, and Toxicology (Munchen). 9(3):210-219, 1974.

The treatment of newborn girls, with birthweights ranging between 2800 and 3800 g, with diazepam and phenobarbitone is described. A group of 31 infants received 0.2mg diazepam per kg bodyweight per day; 27 received 1mg phenobarbitone; and 29 received a placebo. The treatment began when the infants were 36 plus or minus 12 hours of age and was continued during 3 consecutive days and the plasma levels of total bilirubin were followed over 4 days. The treatment decreased the relative bilirubin levels on the second, third, and fourth day. Diazepam appeared the most effective drug. A rather low bilirubin level of the newborn is correlated physiologically with a high birthweight and is more likely to be decreased by drugs. High birthweight, as a rule, is expected to be correlated with a long gestation period. However, a group of neonates characterized by low birthweight, long gestation period, and high bilirubin levels, was most influenced by diazepam. In agreement with other findings, a tendency for high bilirubin levels was found in breast fed children whose mothers had used contraceptive drugs. 9 references. (Author abstract modified)

191677 Iizuka, Reiji; Takahashi, Toshiya. Juntendo University, School of Medicine, Japan **Indication and problems of psychotropic drugs in general practice.** Juntendo Medical Journal (Tokyo). 19(4):542-550, 1973.

A general procedure for diagnosis of psychosomatic diseases and administration of psychotropic drugs in general practice is discussed. The types and etiology of psychosomatic diseases, and the types of psychotropic drugs useful in such cases are considered. 5 references.

191685 Honma, Kenichi; Moroji, Takashi. School of Medicine, Hokkaido University, Japan **Daily rhythm in body temperature of mental patients: application of cosinor method -- first report.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(5):643-651, 1973.

The diurnal rhythm of body temperature in schizophrenics under psychotropic medication, brain-damaged patients not on medication, and in normal adults was examined using Halberg's cosinor method. Body temperature was measured every 4 hours from 6 am to 10 pm for 31 to 43 days. All normals showed a regular diurnal rhythm, while brain-damaged Ss showed a noticeable but sometines irregular diurnal pattern. Diurnal rhythm in schizophrenics under medication was irregular or nonexistent, and not clearly associated with continuation or withdrawal of medication. Chronic schizophrenics showed more irregularities in diurnal rhythm than did acute patients. Further studies are necessary to delineate the relationship of psychotropic medication to modifications in diurnal body temperature patterns. 29 references.

191693 Ishigane, Masaaki; Ito, Kozo. Sapporo Hanazono Hospital, Japan **Psychiatric pharmacology of the aged.** Japanese Journal of Clinical Psychiatry (Tokyo). 2(5):619-625, 1973.

Psychopharmacology for aged patients is discussed. The types of psychotropic drugs, doses and usage of drugs for various illnesses, such as arteriosclerosis, senile dementia, depression, manic state, delusion and neurosis, are considered. The necessity for careful usage of these drugs in order to avoid various side-effects is stressed. 6 references.

192059 Carlson, Eric T. Department of Psychiatry, New York Hospital-Cornell Medical Center, 525 E. 68th Street, New York, NY 10021 **Cannabis indica in 19th-century psychiatry.** American Journal of Psychiatry. 131(9):1004-1007, 1974.

The history and usage of cannabis sativa indica in psychiatric applications in the 19th cnetury is reviewed. The

drug's physiological and psychological effects are reviewed. It is contended that most of the effects reported in the 1960's were known to writers of the 19th century, when the drug was alternately considered a cure for and cause of insanity. 3 references. (Journal abstract modified)

192092 Skousen, W. Cleon. 37 W. 38th St., New York, NY 10018 **LSD and the insanity drugs, part XXXI.** Law and Order. 22(9):32, 34, 36, 38, 40, 42, 1974.

The dangers of hallucinogen abuse, notably LSD, STP, DMT, mescaline, peyote, and psilocybin, are discussed. Promotors of the hallucination drugs maintain they can be used as a means of inducing temporary psychosis and thereby facilitate the study of mental illness or it can be used as a means to great personal insight. However, medical statistics show that instant insanity drugs lead to serious and often tragic consequences. Reactions to hallucination drugs are completely unpredictable and chromosomal and brain damage can be expected from LSD usage.

192410 Campbell, Horace E. Denver, CO **Crime and the sex drive.** Rocky Mountain Medical Journal. 71(7):385-386,1974.

The view that sex is the dominant force that drives nearly all criminals is presented and recommendations are made for how sentencing and treatment should be changed to insure that offenders are cured before their release from prison. Various drug therapies and prison management changes are proposed. 15 references.

192412 Ban, T. A.; Ananth, J. V..; Lehmann, H. E. Douglas Hospital, 6875 La Scalle Blvd., Verdun, Quebec, Canada **Conditioning in the prediction of drug withdrawal effects in chronic schizophrenic patients.** Activitas Nervosa Superior (Praha). 16(1):23-33, 1974.

A 1 year study was designed to identify predictive conditioning variables for drug withdrawal effects on the basis of administration of the Verdun Conditioning Program, in a group of 60 chronic hospitalized schizophrenic patients. The three groups which should be maintained without medication were characterized by relatively superior mean total performance on the battery as a whole and in the skeletomuscular functional system, associated with a relatively impaired performance in the integrational functional system, especially in generalization, compared to the performance of the groups which could not be maintained without medication. 21 references. (Author abstract modified)

192704 Morris, Louis A.; O'Neal, Edgar C. Newcomb College of Tulane University, New Orleans, LA **Drug-name familiarity and the placebo effect.** Journal of Clinical Psychology. 30(3):280-282, 1974.

Sixty four male students were tested to determine whether familiarity with the name of a drug would affect reactions to the drug. All Ss were given placebos. Two placebo labels were familiar names of commonly used drugs, and two were unfamiliar (fictitious) names. Although the suggestions furnished by E and bogus feedback about T's pursuit rotor performance after ingestion of the drug did produce significant results, the familiarity dimension did not produce any reliable effects. Results conform to the response bias model for understanding placebo effects. 9 references. (Author abstract modified)

192787 Small, Ernest; Beckstead, H. D. Plant Research Institute, Dept. of Agriculture, Ottawa, Canada **Common cannabinoid phenotypes in 350 stocks of Cannabis.** Journal of Natural Products. 36(2):144-165, 1973.

Three hundred and fifty diverse seed acquisitions of Cannabis were grown outdoors under uniform conditions in Ottawa, Canada and analyzed for their content of cannabidiol (CBD), delta9-tetrahydrocannabinol (delta9-THC), delta8-THC, cannabigerol monomethyl ether (CBGM) and cannabinol (CBN). Plants originating from countries north of 30 degrees North (N) almost always had higher contents of cannabinoids in the female than in the males. Considerable amounts of CBD were present. Moderate and high amounts of THC were sometimes present in the females. In plants originating from countries south of latitude 30 degrees N, high amounts of THC and low amounts of CBD were frequently present in both sexes. CBN was rarely present in freshly harvested plants and then only in trace amounts. Trace amounts of a compound having the same retention time as CBGM were consistently present in plants originating from northeastern Asia. Tabulations of results are included. 13 references. (Author abstract modified)

AUTHOR INDEX

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